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BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 3 1955

MITRAL VALVE DISEASE AND MITRAL VALVOTOMY

BY

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[WITH SPECIAL PLATE]

Mitral valvotomy has now become a standard surgical procedure, and in recent years a number of reports of the results have appeared in the literature (Baker *et al.*, 1952; Bailey *et al.*, 1952; Logan and Turner, 1953; Sellors *et al.*, 1953; Douglas and Hill, 1954; Wood, 1954).

The object of the following communication is to present clinical details, investigations, and operative findings in 75 patients submitted to mitral valvotomy between December, 1950, and September, 1954, and to analyse the results in 56 of them who have been followed up for periods ranging from six months to three years. Particular emphasis has been paid to the problem of accurate diagnosis of mitral valve disease, and to the association between important symptoms and physical signs, in the assessment of the severity of the stenosis. We also report the clinical findings in 10 patients with severe mitral incompetence associated with stenosis who were submitted to operations for repair of the mitral valve.

The indications for valvotomy are discussed later. The results of valvotomy have been examined critically in the light of the pre-operative picture. It will be realized that this series represents a highly selected group of patients who were considered suitable for mitral valvotomy or valve repair, and the symptoms and physical findings must not be taken as necessarily representing the findings in all cases of mitral disease.

Material and Methods

Of the 75 patients with mitral stenosis, 58 were female and 17 male. Their ages ranged from 17 to 58 years: 48 were between 20 and 40 years, 22 between 40 and 50, 2 were aged 17, and 3 were over 50.

1. Clinical Assessment

Symptoms.—Dyspnoea on exertion was graded as follows:—Grade I: dyspnoea on severe exertion only. Grade II: dyspnoea on moderate exertion, sufficient to interfere with daily life. Grade III: dyspnoea on the least exertion. Grade IV: dyspnoea at rest. The degree of dyspnoea was estimated not only by careful consideration of the history but also by observation of the patient's effort tolerance while in hospital. Attention was also paid to the following: paroxysmal dyspnoea, or orthopnoea; bronchitis; haemoptysis; chest pain on effort; embolic phenomena; and congestive failure.

Physical Signs.—The following were especially noted: the character of the arterial pulse; jugular venous pressure and pulse; apical presystolic or rumbling diastolic murmurs; apical first heart sound; opening snap of the mitral valve; third heart sound; apical systolic murmur; and pulmonary hypertension, assessed according to the following grades (Davies *et al.*, 1953):—Grade O: normal left ventricular impulse, normal second heart sound. Grade I: tapping impulse, gentle sternal lift, narrow splitting of the second heart sound, with slight accentuation of the pulmonary element. Grade II: tapping impulse, marked sternal heave, narrow splitting of the second heart sound, with more accentuation of the second element.

2. Investigations

Radiology.—Fluoroscopy, and radiographs in the postero-anterior, oblique, and lateral projections with barium swallow, were taken, and oblique tomograms were examined for auricular or valvular calcification. The cardiac volume was measured in 65 patients according to the method of Friedman (1951).

Left Auricle.—The size was graded as follows:—Grade O: appendix just visible on the left cardiac border in the postero-anterior film; minimal backward displacement of the barium-filled oesophagus in the left lateral film. Grade I: appendix visible on the left cardiac border in the postero-anterior film, and the contour of the auricle just visible at the right cardiac border; definite backward displacement of the oesophagus in the lateral view. Grade II: marked prominence of the appendix at the left cardiac border and of the left auricle at the right cardiac border; considerable backward displacement of the oesophagus. Grade III: aneurysmal enlargement, the left auricle overshadowing the other cardiac chambers and main pulmonary arteries.

Right Auricle.—This was considered to be enlarged when its right margin could be seen bulging prominently beyond and below the left auricle at the right border of the heart in the postero-anterior film, as in Fig. 5 (Special Plate).

Ventricles.—Enlargement was assessed on fluoroscopy and on lateral films.

Pulmonary Vascular Pattern.—Abnormalities of the pulmonary arterial tree were classified as previously reported (Davies *et al.*, 1953):—Grade O: slight enlargement of the main pulmonary artery only. Grade I: enlargement of the main pulmonary artery, including the first divisions, with narrowing and tortuosity of the distal branches, the changes being confined to the bases of the lungs. Grade II: marked enlargement of the main pulmonary artery and main branches, with more widespread peripheral changes. As has been previously shown (Davies *et al.*, 1953), these grades are a guide to the level of pulmonary arterial pressure (Grade O equivalent to systolic pulmonary artery pressure up to 40 mm. Hg; Grade I, 40–60; Grade II, greater than 60). Accurate estimation of the pulmonary arterial changes was impossible in the presence of marked haemosiderosis or a very large heart. All films were examined for the presence of haemosiderosis, and for fine horizontal lines at the costophrenic angles ("Kerley's lines": Kerley, 1951).

Cardiography.—Multiple lead cardiograms were recorded in all patients, lead V4R being included in most. Right ventricular hypertrophy was graded as previously reported (Davies *et al.*, 1953):—Grade O: normal ventricular complexes with or without abnormal P waves or auricular fibrillation. Grade I: clockwise rotation (R smaller than S in V5), predominant R wave in VR and V4R. Grade II: R wave greater than S in VI and V4R, R wave smaller than S in V5, predominant R wave in VR.

Cardiac catheterization.—This was carried out in 40 patients. Pulmonary hypertension was graded as follows: Grade O: systolic pulmonary artery pressure below 40 mm. Hg. Grade I: systolic pulmonary artery pressure 40–60 mm. Hg. Grade II: systolic pulmonary artery pressure greater than 60 mm. Hg. All patients with Grade II pulmonary hypertension on catheterization were considered to have an increased pulmonary arteriolar resistance, but this was not measured in more than a few subjects.

3. Surgical Assessment

Mitral valvotomy was performed on the majority of patients by one of us (W. P. C.) and on the remainder by one or other of the following associates: Mr. R. Shackman, Mr. Angus McArthur, Mr. L. L. Bromley, Mr. P. Hooton, and and Mr. C. A. Jackson, to whom we are indebted for their findings.

Approach to the mitral valve was via the left auricular appendix in all except one patient (see Results).

The following points were noted: (1) Thrombus or calcification in the left auricle or appendage. (2) Valvular calcification. (3) Size of mitral orifice—the distance between the commissures was estimated by the surgeon's finger as follows: less than 1 cm., 1–1.5 cm., 1.5–2 cm., or more than 2 cm. (4) Presence of mitral incompetence before the split: Grade I—minimal regurgitant puff, which was not of importance; Grade II (+)—if a moderate stream could be felt; and Grade III (++)—if this reached the auricular wall and produced a systolic thrill. (5) The split obtained: the degree was graded as "good" if the final orifice diameter was greater than 2.5 cm., "fair" if 2–2.5 cm., and "poor" if less than 2 cm. (6) Regurgitation after the split: this was sometimes difficult to assess owing to the fact that at this time the patient's cardiac output, blood pressure, and blood flow through the mitral orifice were often reduced, and there was therefore a tendency to underestimate the severity of any regurgitation produced. (7) Biopsy of

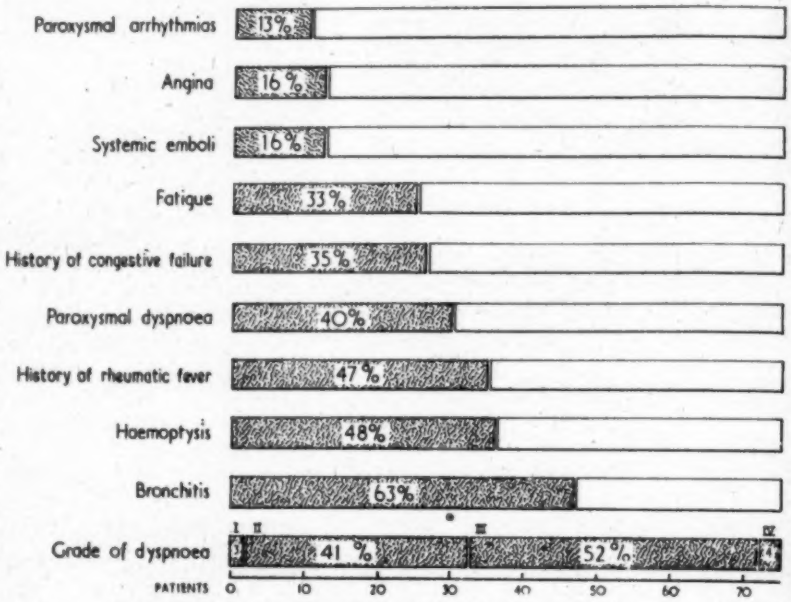

FIG. A.—Symptomatology in 75 patients with mitral stenosis who were submitted to mitral valvotomy.

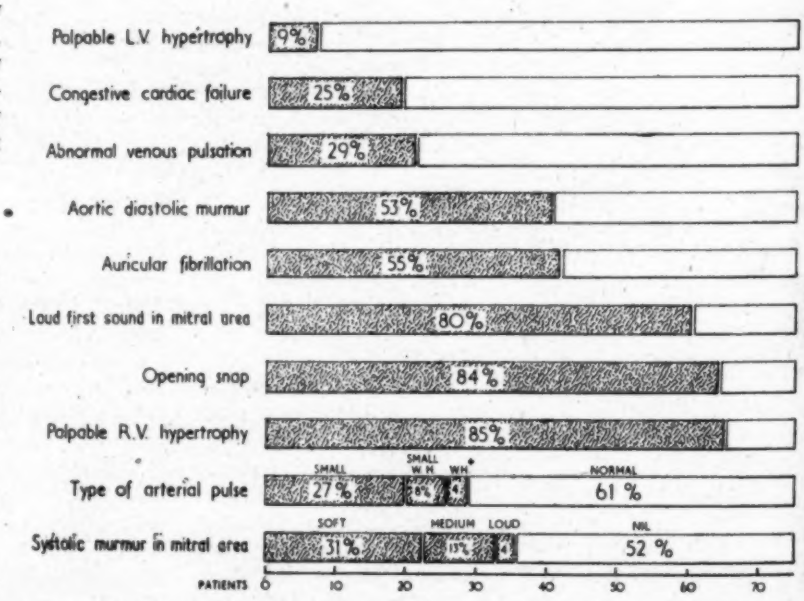

FIG. B.—Physical signs in 75 patients with mitral stenosis who were submitted to mitral valvotomy. L.V.=left ventricle. R.V.=right ventricle. W.H.=water hammer.

left auricular appendage: a specimen was obtained in 56 patients and examined by Professor C. V. Harrison.

The presence of more than six endocardial Aschoff bodies in the section was considered to be evidence of definite rheumatic activity (+); if they were very numerous, marked activity (++).

Pre- and Post-operative Care.—Patients were admitted to hospital one to two weeks before operation, and all were given digitalis. Rigid salt restriction in the immediate pre-operative period was found to predispose to the development of salt deficiency after the operation. An intake of 2–3 g. of sodium chloride and 3 pints (1.7 litres) of fluid was found to be satisfactory for most patients. Chemotherapy with penicillin, and physiotherapy, was started three or four days before operation. Post-operative management did not differ from that used after other thoracic operations, especially with regard to breathing and coughing exercises and the control of bronchial secretions. Care was taken to control the ventricular rate and to avoid cardiac failure, electrolyte imbalance, and pulmonary emboli. Digitalis was continued indefinitely in all patients with auricular fibrillation and in all but a few with sinus rhythm.

Pre-operative and Operative Findings in 75 Patients Submitted to Mitral Valvotomy

The assessment of patients with mitral stenosis demands a study of all the factors which may help to arrive at an estimate of the size of the mitral orifice and its suitability for valvotomy.

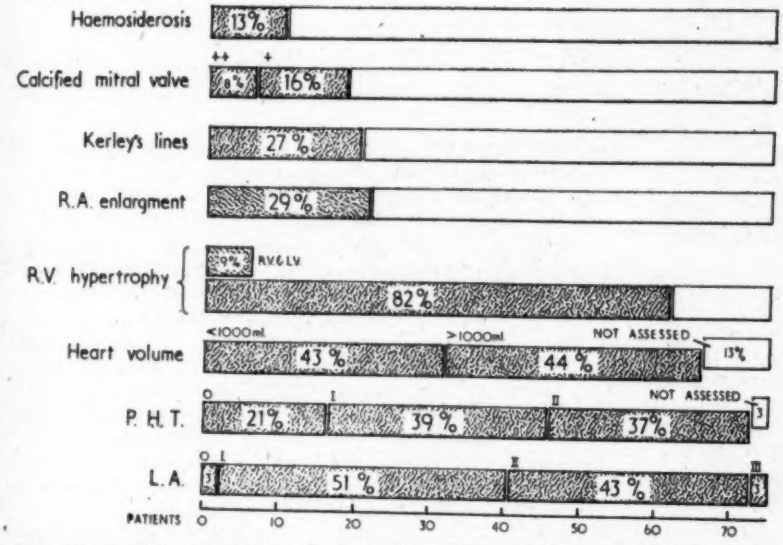

FIG. C.—Radiological findings in 75 patients with mitral stenosis who were submitted to mitral valvotomy. R.V.=right ventricle. P.H.T.=pulmonary hypertension. L.A.=left auricle. R.A.=right auricle.

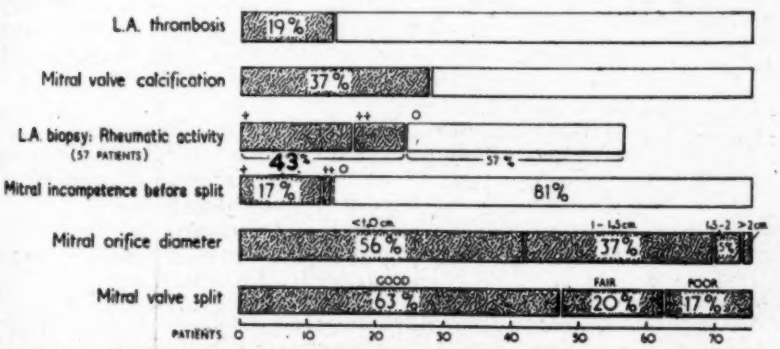

FIG. D.—Operative findings in 75 patients with mitral stenosis. L.A.=left auricular.

The symptomatology and physical signs and the radiological, cardiographic, and operative findings are set out in Figs. A–D.

1. Symptoms

We have examined the relation between each of the four main symptoms—dyspnoea on effort, bronchitis, haemoptysis, and paroxysmal dyspnoea respectively—and the diameter of the mitral orifice found at operation.

TABLE I.—*Grade of Dyspnoea and Valve Size in 75 Patients submitted to Mitral Valvotomy*

Valve Orifice Size	Grade of Dyspnoea			
	I	II	III	IV
>2 cm.	1	0	0	0
1·5–2 cm.	1	0	3	0
1–1·5 cm.	1	17	7	3
<1 cm.	0	12	30	0

$\chi^2 = 6.50$.

TABLE II

Valve Size: (No. of Patients):	>2 cm. (1)	1·5–2 cm. (4)	1–1·5 cm. (28)	<1 cm. (42)
Paroxysmal dyspnoea ..	0	3	11	16
Bronchitis	1	1	19	26
Haemoptysis	1	0	11	24

Table I sets out the relationship of grades of dyspnoea to the diameter of the mitral orifice, and shows that the severity of the dyspnoea tends to be inversely proportional to the size of the valve. This correlation is significant ($\chi^2 = 6.50$), although there is some overlap, and three of four patients with larger mitral orifices had Grade III dyspnoea.

Table II shows that the incidence of paroxysmal dyspnoea, bronchitis, and haemoptysis was not increased by any further narrowing beyond the critical size of 1.5 cm., but it should be noted that paroxysmal dyspnoea occurred in three of the four patients with an orifice diameter of 1.5–2 cm., which supports the findings of Wood (1954) that this symptom does not necessarily occur only with the severest degrees of stenosis.

Pain suggestive of angina of effort was a feature in 12 (16%) of the patients. In one patient an effort test was performed and was positive. Of these 12 patients, 10 had severe (Grade II) radiological pulmonary hypertensive changes, and in 7 the orifice diameter was less than 1 cm. One patient had systemic hypertension and one had slight aortic valve disease. We agree with Wood (1954) that the pain probably represents myocardial ischaemia secondary to low cardiac output and reduced left ventricular filling, and the high incidence of very small mitral orifices and severe pulmonary vascular change in these patients supports this view.

2. Physical Findings

Arterial Pulse.—This was normal in volume in 61% of patients, and small in 27%. No patient with a mitral orifice larger than 1.5 cm. in diameter had a small pulse, but patients with an orifice of less than 1 cm. frequently had a normal pulse. In this series the pulse was not of much value in assessing the size of the mitral orifice, although a small pulse suggested a tight stenosis. All the patients with a water-hammer pulse had aortic incompetence.

Auricular Fibrillation.—Fibrillation was slightly more common in patients with an orifice of 1–1.5 cm. (13 of 27) than in those with orifices of less than 1 cm. (27 of 42).

Abnormal Venous Pulsé Form.—Eight patients had an augmented presystolic "a" wave in the jugular venous pulse. All had Grade II or III dyspnoea on exertion. Six had clinical and radiological, and seven cardiographic, evidence of severe (Grade II) pulmonary hypertension, which was confirmed in the five who were subjected to cardiac catheterization. The mitral orifice was less than 1 cm. in six, and 1–1.5 cm. in two. In four the right auricle was enlarged radiologically, but in no case was evidence of tricuspid stenosis found, although this might have been missed in two patients in whom catheterization was unsuccessful. We have concluded that an augmented cervical "a" wave, when present, indicates tight mitral stenosis and severe pulmonary hypertension, although the possibility of tricuspid stenosis must be seriously considered if signs of pulmonary hypertension are absent (Wood, 1954).

Some degree of tricuspid incompetence was diagnosed in 14 patients who had a large systolic wave in the jugular venous pulse. All these patients had Grade III or IV dyspnoea and evidence of moderate or severe pulmonary hypertension. All except two patients had auricular fibrillation, and the cardiograph showed marked right ventricular hypertrophy in six, and right bundle-branch block in one. The right auricle was enlarged in seven; nine had the smallest valve size.

Mitral First Sound and Opening Snap.—The importance of a loud mitral first sound and opening snap as indications of a mobile valve has been stressed by Sellors *et al.* (1953). These signs were present in most of our patients, but the opening snap was absent in 11, and the mitral first sound not accentuated in 15. The association of absent opening snap with a soft mitral first sound occurred in six patients; five of these had severe (Grade II) radiological hypertension (one could not be assessed), and four had heavily calcified valves. Of 15 patients with a soft mitral first sound, pulmonary hypertension was not a significant feature; only five had calcified valves, but seven had slight and one severe mitral incompetence. We have concluded that a soft mitral first sound and absent opening snap indicate a rigid valve, significant mitral incompetence, or, less frequently, severe pulmonary hypertension.

Apical Systolic Murmur.—This was present in 48%, and was recorded clinically as soft in 31%, medium in 13%, and loud in 4%. It was invariably maximal at the apex, conducted to the axilla, and decreased on inspiration. A soft murmur was noted in 23 patients, only one of whom had a mitral orifice of more than 1.5 cm. A murmur of medium intensity was noted in 10 patients, and again the orifice was greater than 1.5 cm. in only one patient. The loud murmur which was heard in three patients was associated with an orifice of less than 1 cm. in two, in whom there was no evidence of mitral incompetence at operation. Slight incompetence was found at operation in three patients who had no systolic murmur and in six who had a medium systolic murmur. By contrast, incompetence was absent in four patients with the same medium intensity murmur. The only patient who had severe mitral incompetence had a loud systolic murmur at the apex. We consider that a soft or medium systolic murmur is not necessarily an indication of significant incompetence.

Right Ventricular Hypertrophy.—Some degree of right ventricular hypertrophy was present in all but 12 (15%) of the patients.

3. Radiological Findings

Pulmonary Hypertension.—We have previously suggested (Davies *et al.*, 1953, 1954) that radiological evidence of severe pulmonary hypertension is usually associated with severe mitral valve disease, and have therefore examined this relationship (Table III). There is a tendency for Grade II *x*-ray changes to be associated with the smallest valves (χ^2 = 3.77, which is just below the usual significance level).

TABLE III.—*Radiological Pulmonary Hypertension and Valve Size in 73* Patients submitted to Mitral Valvotomy*

Radiological Grade of Pulmonary Hypertension	Valve Orifice Size			
	>2 cm.	1·5–2 cm.	1–1·5 cm.	<1 cm.
O	1	2	10	3
I	0	1	10	18
II	0	1	7	20

* Two were not assessed radiologically. $\chi^2 = 3{\cdot}77$.

TABLE IV.—*Catheter Grade of Pulmonary Hypertension and Radiological Grade of Pulmonary Hypertension in 37 Patients*

Radiological Grade of Pulmonary Hypertension	Catheter Grade of Pulmonary Hypertension		
	O	I	II
O (normal) ..	1	5	0
I (moderate) ..	1	11	3
II (severe) ..	0	1	15

Table IV shows the association between the radiological estimation and catheter measurement of pulmonary hypertension. Our findings suggest that the more severe the stenosis the greater the pulmonary vascular change, although there is naturally some overlap, for it will be noted from Table III that radiological evidence of pulmonary hypertension was absent in 13 of 70 patients with critically small valves. Table V shows the relationship between pulmonary vascular change and grade of dyspnoea, and there is a significant correlation (χ^2 = 7.30). It will be seen, therefore, that both severe (Grade III) dyspnoea and severe (Grade II) radiological pulmonary vascular changes usually indicated a very small valve.

TABLE V.—*Grade of Dyspnoea and Grade of Pulmonary Hypertension in 73* Patients submitted to Mitral Valvotomy*

Radiological Grade of Pulmonary Hypertension	Grade of Dyspnoea			
	I	II	III	IV
O (normal) ..	2	9	5	0
I (moderate) ..	0	14	15	0
II (severe) ..	0	6	20	2

* Two were not assessed radiologically. $\chi^2 = 7{\cdot}30$.

Other Radiological Changes (Fig. C).—The right ventricle was enlarged in all except 13 patients, while the left ventricle was enlarged only in patients with associated aortic disease, and in one subject with systemic hypertension. Enlargement of the left auricle was Grade I or II in nearly all patients, but was aneurysmal in two, of whom one had clinical and operative evidence of tight stenosis, and the other presented signs suggestive of predominant incompetence, but was found to have mainly stenosis at operation. Calcification was detected in 18 patients, but was not seen in 10 others in whom slight calcification was found at operation. Calcification which did not show on tomography was of practical significance in only one patient, who had a very large heart. Extensive radiological mitral valve calcification was seen both with and without slight incompetence. Calcification in the left auricular appendage was detected in one patient and pericardial calcification in another.

Haemosiderosis.—This was present in 10 patients, of whom six had severe and four had moderate pulmonary hypertension; it was also associated with haemoptysis, Grade III dyspnoea, and the smallest mitral orifices.

Kerley's Lines (Special Plate, Figs. 1 and 8).—These were present in 20 patients, and showed the same relationship to pulmonary hypertension and valve size as did haemosiderosis. They were not seen without other evidence of pulmonary hypertension, and were sometimes transient.

Heart Volume.—There was no significant correlation between valve size and heart volume.

4. Cardiography

There was no significant correlation between the cardiographic grade of right ventricular hypertrophy on the one hand and size of the mitral orifice or the degree of

pulmonary hypertension on the other (Fig. E). Indeed, 15 patients with orifices of less than 1 cm. diameter and 15 with 1–1.5 cm. orifices had no evidence of right ventricular hypertrophy. Only 5 of these 30 patients had clinical or radiological evidence of left ventricular hypertrophy due to aortic valve disease which might obscure the evidence of right ventricular hypertrophy. Right bundle-branch block was present in two patients. The presence of definite right ventricular preponderance is suggestive evidence of critical stenosis, but may also occur with important incompetence, as is shown later (Table VII). This is probably due to the fact that right ventricular hypertrophy is dependent upon pulmonary hypertension which may complicate severe mitral incompetence as well as stenosis.

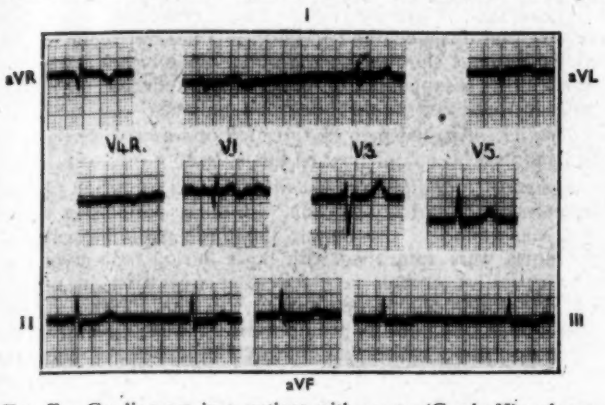

FIG. E.—Cardiogram in a patient with severe (Grade II) pulmonary hypertension (measured by cardiac catheterization). There is minimal evidence of right ventricular hypertrophy: rSR′ (R′=S) in Lead V1, Qr in VR, Rs in V5. Indeterminate pattern in V4R. Auricular fibrillation. Digitalis effects.

5. Operative Findings (Fig. D)

Ninety-three per cent. of patients had critical valve orifices (less than 1.5 cm. diameter), and a good or fair split was obtained in the majority. Slight mitral incompetence was present before valvotomy in 13 patients and severe incompetence in only one. Slight incompetence was produced in 12 patients and marked incompetence in 4. There was thrombus in the left auricle in 14 patients, all of whom had auricular fibrillation, but in only three was there a history of emboli. And, as is shown later, the converse was also true.

The valve was calcified in 28 (37%) patients, 18 of these having no mitral incompetence, and the remainder slight incompetence. Table VI shows the relation of calcification of the valve to the split obtained.

TABLE VI

Valve Calcification at Operation	Split		
	Good	Fair	Poor
0	32	6	9*
+	13	7	2
++	2	2	2

* Most of the 9 patients without calcification who had a poor split were patients operated upon early in the series, before the surgical technique had been perfected.

There was evidence of rheumatic activity in 43% of 56 subjects in whom a left auricular biopsy was examined.

Approach to the mitral valve was rendered impossible in two patients because of thrombotic occlusion of the left auricular appendage and calcification of the auricular wall. A slight excess of pericardial fluid was a frequent finding, but in only one instance was a large effusion encountered. Pericardial adherence was surprisingly infrequent.

A further patient, in whom calcification of the pericardium had been detected radiologically, was found to have a rigid plate of calcium over the right auricle. When this was removed the patient's condition improved significantly, with a rise in blood pressure and an increase in pulse volume. Valvotomy was completed without incident, and the final clinical result was excellent. Biopsy of the pericardium revealed no evidence of tuberculosis.

Biopsy of the lingula was carried out in a number of patients, but did not yield any important information.

Diagnosis of Mitral Incompetence

The signs usually taken to indicate important mitral incompetence are: a medium or loud pansystolic murmur, blowing in quality, conducted to the axilla and decreasing on inspiration (Biörck *et al.*, 1953; Müller and Shillingford, 1954); a soft first heart sound; a large left ventricle; and a very large left auricle. The opening snap is usually absent, and is replaced by a third heart sound (Brigden and Leatham, 1953; Wood, 1954). Recently the importance of a small and water-hammer type of arterial pulse and a hyperdynamic left ventricle has been stressed (Wood, 1954).

Table VII shows our findings in the 10 patients in whom mitral stenosis with important mitral incompetence was diagnosed clinically. The diagnosis was confirmed at operation for correction of the lesion.

TABLE VII

	No. of Patients
Mitral systolic murmur	10 (loud, 4; medium, 5; soft, 1)
Water-hammer pulse	8 (small volume in 4 of these), 7 had aortic incompetence
Left ventricular hypertrophy	9 (but also R.V.+ in all)
Mitral diastolic murmur	10
Accentuated mitral first sound	7
Opening snap of mitral valve	9
Third sound	1
Left auricular enlargement	10 (aneurysmal, 3; grade II, 5; grade I, 2)
Mitral valvular calcification	1
Radiological pulmonary hypertension	Severe, 2. Moderate, 1. Nil, 1 (4 could not be assessed owing to a very large heart)
Cardiograph	R.V.+5. L.V.+0. Neither R.V.+ nor L.V.+ 5

Cardiac catheterization was performed in six patients: one had severe, three had moderate, and the remainder had no pulmonary hypertension. The symptoms did not differ from those found in patients with pure mitral stenosis. We have found the most helpful association of signs indicating mitral incompetence to be the typical systolic murmur, enlargement of the left ventricle, and considerable or aneurysmal enlargement of the left auricle. But these signs, with the exception of left ventricular hypertrophy, have been found separately in pure or predominant mitral stenosis. We are uncertain of the value of the water-hammer pulse in the diagnosis of mitral incompetence, especially as many such patients also have aortic insufficiency. We have not found the absence of the opening snap to be of value in differentiating between predominant incompetence and stenosis, but differentiation between a third heart sound and opening snap may be difficult without phonocardiography, since the third sound in mitral incompetence occurs early (Wood, 1954). We have not been impressed with the value of the pulmonary capillary venous pulse form in the diagnosis of incompetence, and agree with Wynn *et al.* (1952) and with Venner and Holling (1953) that it may be similar in mitral incompetence and in mitral stenosis. Recently Owen and Wood (1954) have reported the value of the RY/V ratio of the pulmonary capillary venous pulse in the diagnosis of incompetence.

The difficulties in the diagnosis of mitral incompetence are illustrated by the following two cases.

Case K. K.—This patient was a Polish woman aged 24. She had Grade III dyspnoea on effort, a history of paroxysmal dyspnoea, congestive heart failure, and substernal pain on exertion. On examination she was found to have auricular fibrillation; her pulse was normal in type. There was a loud apical systolic murmur and a rumbling diastolic murmur; an opening snap was present, but the first sound was not accentuated. There were aortic systolic and diastolic murmurs, and the second heart

sound at the base was split and the pulmonary component was accentuated. The right but not the left ventricle was enlarged clinically. Radiography showed definite left ventricular enlargement, and the left auricle was graded as II. The cardiograph did not show either right or left ventricular hypertrophy. Cardiac catheterization revealed severe (Grade II) pulmonary hypertension. The apical systolic murmur and left ventricular hypertrophy were thought to be due to the aortic lesion. At operation a severely incompetent mitral valve measuring 1.5–2 cm. in diameter was found. Valvotomy did not diminish the incompetence, and the patient died four months later in congestive failure.

Case T. S.—A man aged 34 had Grade IV dyspnoea and congestive heart failure. On examination there was auricular fibrillation; the pulse was normal in volume and slightly collapsing in character. Both ventricles were considerably enlarged. The mitral first sound was not accentuated, and there was no opening snap. There was a medium apical systolic murmur, and a long rumbling diastolic murmur and thrill. The second heart sound was accentuated. There were aortic systolic and diastolic murmurs, and tricuspid incompetence was present. On fluoroscopy the heart was enormously enlarged, the left auricle being aneurysmal and all other chambers enlarged (Fig. 1). The cardiograph showed left ventricular hypertrophy. A diagnosis of mitral stenosis with severe incompetence was made. At operation for mitral valve repair the valve was found to be calcified, was 1–1.5 cm. in diameter, and had a slight regurgitant stream. Hence, a valvotomy only was performed, and a fair split obtained which did not increase the incompetence. The left ventricular enlargement must have been referable to the aortic lesion, and the soft first sound and absence of the opening snap to the calcification of the mitral valve, which had not been detected pre-operatively because of the great size of the heart.

In the first case the correct diagnosis could have been made, but in the second it is difficult to see how this could have been possible.

Results of Mitral Valvotomy

The results were judged by improvement in the patients' dyspnoea, and were classified as follows:—Good: marked increase in effort tolerance—for example, able to do housework or pursue full-time employment when this had been impossible before. Fair: definite improvement in exercise tolerance but still restricted—for example, able to do part-time work. Poor: exercise tolerance unchanged. Development of definite tricuspid incompetence or of congestive heart failure requiring mercurial diuretics.

Patients have been followed for periods of up to three years, the results being set out in Tables VIII and IX. The results in patients upon whom valvotomy was performed less than six months before this analysis was made have not been assessed, as we believe that this period is too short. The total mortality was 12% (Table X). There are 41 patients available for assessment at one year, and further assessment has been made of 11 at two years, and of 5 at three years. No detailed analysis of the effect of the operation on individual signs and symptoms has been made on the 15 patients followed for only six months.

TABLE VIII.—*Symptomatic Results of Mitral Valvotomy in 75 Cases*

Time Patients Followed Up	No. of Patients	Result			
		Good	Fair	Poor	Dead*
(a) 3 years ..	5	2	—	3	—
(b) 2 ,, ..	11	7	3	1	—
(c) 1 year ..	25	18	4	1	2
(d) 6 months ..	15	8	4	1	2
(e) Less than 6 months ..	19	Not assessed			5

* See Addendum.

TABLE IX.—*Symptomatic Results at One Year after Valvotomy*

No. of Patients	Good	Fair	Poor	Dead*
41 (a+b+c at 1 year)	26	10	3	2

* See Addendum.

TABLE X.—*Total Mortality (See Addendum)*

Hospital mortality*	4 patients
In first 6 months	3 ,,
,, ,, 6–12 months	2 ,,
	9 ,,

* Denotes death at operation or before discharge.

Effect of Valvotomy in the 41 Patients at 1 Year

Paroxysmal Dyspnoea, Bronchitis, and Haemoptysis.—Paroxysmal dyspnoea and haemoptysis did not recur in any of the patients showing good results, while attacks of bronchitis either disappeared or were greatly reduced in severity both in these and in the fair-result patients.

Angina.—Anginal pain disappeared or was greatly reduced in patients who complained of this symptom pre-operatively.

Systemic Emboli.—No systemic emboli occurred during or immediately after operation. In many patients in whom clot was found in the auricle the three main branches of the aorta were controlled with tapes during the valvotomy. Post-operative emboli recurred after operation in only 1 of 12 patients with a pre-operative history. This patient had a small embolus in the right radial artery several weeks after operation, which was followed by rapid and complete recovery. One other patient, who had no previous history of emboli, had a cerebral embolus three days after operation which resulted in a transient hemiparesis.

Pregnancy.—Operation was performed during pregnancy in two patients—in one because of attacks of paroxysmal dyspnoea at three months, and in the other because of persistent dyspnoea at rest at five months. Valvotomy was successful in both patients; the symptoms were relieved, the pregnancy remained undisturbed, and delivery of a normal child was uneventful in each instance.

Congestive Cardiac Failure.—This did not recur in 10 of 11 patients who required mercurial diuretics for a period pre-operatively.

Tricuspid Incompetence.—Tricuspid incompetence, which was present in seven patients before operation, disappeared in five. Four patients developed tricuspid incompetence after operation (Table XI).

TABLE XI.—*Tricuspid Incompetence* (11 *Cases*)

	Result			
	Good	Fair	Poor	Dead
Disappeared ..	3	2	—	—
Unchanged ..	—	—	1	1
Developed ..	—	2*	2	—

* These two patients were classified as having a fair result because their effort tolerance had improved and they had no signs of congestive failure.

Auscultatory Signs of Mitral Stenosis.—These signs consisted of an accentuated first sound at the apex, a presystolic murmur, a rumbling diastolic murmur, and an opening snap. There was a decrease in at least two of the signs in only nine of the patients, eight of whom had a good result. The remaining 18 of the 26 patients who had a good result showed no alteration in these signs.

Clinical Signs of Pulmonary Hypertension.—The signs of pulmonary hypertension were unchanged in over half the patients, and the result was good or fair in the majority of these. In the 13 in whom signs decreased the result was good in 11 and fair in 2 (Table XII).

TABLE XII.—*Changes in Clinical Signs of Pulmonary Hypertension One Year After Operation*

	No. of Patients	Result			
		Good	Fair	Poor	Dead
Decreased ..	13	11	2	—	—
Unchanged ..	26	14	7	3	2
Increased ..	2	1	1	—	—

Mitral Systolic Murmur.—This murmur appeared post-operatively in four, increased in nine, decreased in two, and disappeared in four. The relationship of a mitral

systolic murmur to the result is shown in Table XIII, and it is apparent that changes in a mitral systolic murmur did not necessarily bear a relationship to the result.

TABLE XIII

	Results			
	Good	Fair	Poor	Dead
Murmur appeared	2	1	—	1
,, increased	4	3	2	—
,, decreased ..	1	—	1	—
,, disappeared ..	3	1	—	—

Cardiograph.—Satisfactory pre- and post-operative tracings were available in 32 patients. The pattern was unchanged in 20, but showed signs of diminished right ventricular hypertrophy in 12 (Figs. G and H). The relationship of the change in cardiographic appearances to the result is shown in Table XIV.

TABLE XIV

	Results			
	Good	Fair	Poor	Dead
Signs of RV+ unchanged ..	12	4	3	1
,, ,, RV+ decreased* ..	11	1	0	0

* In addition, right bundle-branch block, which was present before operation in two patients, did not alter after valvotomy.

Radiological Features.—Table XV shows the alterations in heart volume among 36 of 41 patients in whom these measurements were available. A change of less than 100 ml. was not considered significant. It will be seen that nearly half the patients showed no change in cardiac volume, but that of 10 patients in whom the heart size decreased, 9 had a good and 1 a fair result (Plate, Figs. 2 and 3).

TABLE XV

Heart Volume	Results		
	Good	Fair	Poor
Unchanged	10	3	2
Increased	4	3	4
Decreased	9	1	—

Enlargement of Right Auricle.—Right auricular enlargement was present in 17 patients before operation. The right auricle decreased in size in six after valvotomy, in all of whom a good result was obtained. Enlargement of this chamber developed in four patients following operation; two of these had a good result and one a poor result; the fourth patient died (Plate, Figs. 4 and 5).

Enlargement of Left Auricle.—Assessment of the size of the left auricle post-operatively was rendered difficult by amputation of the appendage. There was an increase in size in two patients and a decrease in four, but in the majority there was no change.

Radiological Evidence of Pulmonary Hypertension.—A decrease in the appearances of pulmonary hypertension occurred in only nine patients (Plate, Figs. 6 and 7). The relationship of these changes to the results is shown in Table XVI. Kerley's lines disappeared in 5 of 14 patients (Plate, Figs. 8 and 9).

TABLE XVI

Radiological Changes of Pulmonary Hypertension	Result of Valvotomy			
	Good	Fair	Poor	Dead
Unchanged	16	7	3	2
Decreased	7	2	—	—
Increased	1	—	—	—

Three patients were not assessed.

Results Two Years After Valvotomy

Sixteen of our 41 patients have been assessed again at two years after operation. There was no change in the result in 11, 3 improved further, and 2 became worse.

Congestive cardiac failure developed in four patients; two of these had a poor result, but in the other two the result was considered to be fair, since failure was transient and resolved completely. Change in the jugular venous pulse occurred in four patients, indicating the development of tricuspid incompetence in two and its disappearance in two others. The signs of mitral stenosis diminished in three patients, while a mitral systolic murmur disappeared in three, became louder in one, and diminished in one. There was no change in the cardiac rhythm, nor any further significant radiological alterations.

Results Three Years After Valvotomy

Five of our 16 patients have been assessed again at three years; the results in three are poor, and are considered in detail later in an analysis of the poor results in the total series (Table XVIII).

Relationship of Pre-operative Findings to the Results in 41 Patients after One Year

This analysis is shown in Table XVII. All the 14 patients with Grade II dyspnoea, but less than half of those with Grade III dyspnoea, had a good result. A good result followed an apparently poor split in four patients. By contrast, a poor or fatal result followed a good split in four patients, in two of whom some incompetence was produced at operation.

TABLE XVII

Pre-operative Findings	Results in 41 Patients 1 Year After Valvotomy			
	Good (26)	Fair (9)	Poor (4)	Dead (2)
Age { under 40 years	20	4	3	2
Age { over 40 ,, ...	6	5	1	0
Dyspnoea { Grade II	14	0	0	0
Dyspnoea { ,, III	12	9	4	2
Paroxysmal dyspnoea	7	4	1	1
Signs of C.C.F.	7	2	0	0
Auricular fibrillation	13	8	2	1
Tricuspid incompetence (pre-op.) ..	3	2	1	1
Aortic lesions (slight)	18	5	2	0
X-ray: Pul. hypertension { 0 ..	5	2	0	0
X-ray: Pul. hypertension { I ..	11	3	1	0
X-ray: Pul. hypertension { II ..	10	4	2	2
Heart volume { ≤ 1,000 ml. ..	12	4	2	2
Heart volume { > 1,000 ,, ...	14	5	1	0
Valve size { < 1 cm.	18	7	4	2
Valve size { 1–1½ cm.	8	1	0	0
Valve size { 1½–2 cm.	0	1	0	0
Mitral incomp. at operation { befores split { (all slight)	3	3	0	1
Mitral incomp. at operation { after split { slight ..	6	3	2	0
Mitral incomp. at operation { after split { severe ..	0	1	0	2
Calcified valve	8	5	2	2
Split { Poor	4	1	1	1
Split { Fair	6	2	0	0
Split { Good	16	6	3	1
Biopsy—rheumatic activity { 0 ..	10	6	1	1
Biopsy—rheumatic activity { + ..	10	1	1	0

Relationship of Pre-operative Findings to the Results in 15 Patients Followed for at Least Six Months

We have made a similar analysis of the 15 patients who have been followed for only six months after operation. The results are substantially the same as in the 41 patients analysed at one year, although of 10 patients with Grade II dyspnoea only six had good results, three fair, and one poor. Assessment was difficult at this stage because of paroxysmal auricular fibrillation in one, obesity in another, and emotional crises in the third. None of these factors will necessarily prevent a good result at a later date. In the single patient with a poor result, gross mitral incompetence was produced at operation and severe congestive failure was present post-operatively.

Immediate Post-operative State

Cardiac Rhythm.—Thirteen of 34 patients who were in sinus rhythm before the operation developed auricular fibrillation in the immediate post-operative period. With four exceptions all reverted to sinus rhythm either spontaneously or by treatment with quinidine or procaine amide. Ten of the 34 patients pre-operatively in sinus rhythm were

given prophylactic procaine amide or quinidine, but there was no evidence that these measures helped to prevent fibrillation. Four more patients developed auricular fibrillation between one and five months after operation. By contrast, only one of the 41 patients with established auricular fibrillation before operation was reverted and maintained in sinus rhythm afterwards, but in most of them the arrhythmia had been present for long periods and reversion was therefore seldom attempted (Sellors *et al.*, 1953).

"Pericarditis."—A pericardial friction rub was almost the rule; it was related to trauma and the presence of blood in the pericardial sac. This was probably the cause of the T-wave inversion in the cardiograph, which persisted for several weeks or months in some patients.

Congestive Cardiac Failure, Pulmonary Oedema, and Infarction.—Some degree of failure occurred transiently in 12 patients, but did not prevent a good result later. Pulmonary infarction occurred in four patients. Pulmonary oedema was infrequent but of grave omen, usually being associated with the production of severe mitral incompetence at operation, or failure to split the valve in severe cases.

TABLE XVIII.—*Analysis of Pre-operative and Operative Factors in Patients with Poor Results (see also Addendum)*

Patient	Sex	Age	Grade of Dyspnoea	Cong. Failure	Parox. Dysp.	T.I.	Aur. Fib.	Pul. Artery Press. (mm. Hg)	*X*-ray Grade Pul. H.T.	Cardiac Volume (ml.)	Diameter of Mitral Orifice	Calcium (+ or ++)	Surgical Assessment of Mitral Incompetence		Split	L.A. Biopsy Rheum. Activity	Suggested Reasons for Poor Results
													Before Split	After Split			
I. B.	F	32	III	+	+	+	+	–	II	1,330	<1 cm.	+	–	+	Good	+	Severe failure before operation; mitral incompetence produced; valvotomy done too late
A. G.	F	53	III	+	–	–	+	56/35	II	1,160	<1 cm.	+	–	–	„	–	Early in series. Suspected coronary artery disease
A. W.	F	28	III	+	–	–	–	78/14	I	860	<1 cm.		–	–	„	–	Early in series. Congestive heart failure before operation
B. M.	F	38	III	–	+	–	–	63/23	II	930	<1 cm.	++	+	+	Fair	+	Heavy calcification, rigid valve, inadequate split —? re-stenosis
N. Q.	F	40	III	+	–	+	–	–	II	1,000	1–1½ cm.	–	–	–	Good	–	Congestive heart failure with tricuspid incompetence before operation. Valvotomy done too late
E. G.	F	51	II	+	–	+	+	–	O	>1,000	1–1½ cm.	–	–	++	„	0	Severe mitral incompetence produced at operation

L.A. biopsy: – = Not done. 0 = Negative. + = Present.

TABLE XIX.—*Analysis of Pre-operative and Operative Factors in Patients who Died after Mitral Valvotomy (see also Addendum)*

	Age	Grade of Dyspnoea	Congestive Failure	Paroxysmal Dyspnoea	Tricuspid Incompetence	Auricular Fibrillation	Pulmonary Artery Pressure (mm. Hg)	*X*-ray Grade of Pul. Hypertension	Cardiac Volume (ml.)	Diameter of Mitral Orifice	Calcium + or ++	Surgical Assessment of Mitral Incomp.		Split	L.A. Biopsy (Rheum. Activity)	Survival after Operation	Mode of Death	Necropsy Confirmation of Operative Findings	Comments
												Before Split	After Split						
W. D.	43	3	0	0	0	+	76/30	1	1,170	<1 cm.	+	0	++	Good	0	5 mths.	Progressive failure	Not obtd.	Production of mitral incompetence surgically
J. H.	37	4	+	+	+	+	–	2	1,740	1–1½ cm.	++	+	+	? Good	0	1 week	Pul. oedema and congest. failure	+	Operation too late. Heavily calcified valve; severe stenosis; ? adequate split
A. K.	39	3	0	+	0	+	39/7 (R.V.)	2	1,200	<1 cm.	0	0	0	Poor	–	24 hrs.	Vent. fib. during op.; remained in coma afterwards	+	First patient to be operated upon
K. K.	24	3	+	+	0	+	60/30	2	1,440	1½–2 cm.	0	++	++	Poor	+	4 mths.	Prog. congest. failure	+	Error in diagnosis; valve incompetent and unsuitable for valvotomy. Some rheumatic activity confirmed at necropsy
F. L. M.	50	3	0	+	0	+	44/22	0	960	1½–2 cm.	0	+	+	Fair	–	6 weeks	*Ps. pyocyanea* endocarditis	+	Technical difficulties resulted in splitting of auricular wall. Sutures involved left descending coronary; infection introduced with stitch abscess and endocarditis
F. M.	33	3	0	+	+	+	43 (mean)	2	–	<1 cm.	+	+	++	Good	0	11 mths.	Prog. cong. failure	+	Multiple factors. Mitral incompetence increased. Early in series
M. O'M.	36	3	0	0	0	–	80 (mean)	2	1,110	<1 cm.	++	0	+	Poor	–	10 „	Pul. oedema and congest. failure	+	Unsuitable valve, heavily calcified. No split
D. P.	59	3	0	+	0	–	–	2	780	<1 cm.	++	0	+	Good	0	5 „	Failure, pul. embolism, and thrombosis, myocardial infarction	+	Associated coronary artery disease; age of patient perhaps important. Valve split in spite of heavy calcification, but cusps: orn
J. U.	44	4	+	+	0	+	120/5 (R.V.)	2	–	1–1½ cm.	–	0	0	„	+	Death on table	Ventric. fib.	+	Technical difficulties; tear of auricular wall with haemorrhage. Early in series. Some rheumatic activity confirmed at necropsy

Purulent Bronchitis.—This was one of the most serious complications, especially in patients with previous bronchitis. The importance of encouraging full mobility of the patient with breathing and coughing exercises, especially during the first few post-operative days, cannot be emphasized too strongly. Established infection was always controlled by antibiotics, although sometimes with difficulty, as was the case in one patient who developed a fungus infection of the lung, from which she made a slow but complete recovery.

Electrolyte Imbalance.—Apart from salt deficiency in a few patients early in the series, whose pre-operative intake had been too rigidly restricted, electrolyte disturbances were never of importance.

"Post-valvotomy Syndrome."—A clinical picture including fever, anterior chest pain, reappearance of pericardial friction, and increase in jugular venous pressure occurred in seven patients. These symptoms and signs were occasionally associated with radiological evidence of an increase in heart size. Recovery was uneventful in all patients, and one may have benefited from large doses of salicylates. The condition was similar to the "post-valvotomy syndrome" described by Soloff *et al.* (1953), but we have no proof that it was due to a recurrence of rheumatic carditis. In two patients typical acute rheumatism developed within four months of operation. In one of these, aortic incompetence developed. Neither showed any evidence of active rheumatism prior to operation, and both did well.

Analysis of Pre-operative and Operative Factors in Patients with a Poor Result or who Died

In the group of 56 patients who have been followed for six months or more, six patients are now considered to have had a poor result. Two patients did not improve after the operation and subsequently deteriorated further. In two others the results were classed as fair after the operation but became poor at one year. The remaining two initially had a good result, declined to fair at a year, remained in this state for a further year, but became poor at the end of the third year. Three of the five patients who have been followed for three years now show poor results, but the number is too small to allow any general conclusion.

We have attempted to ascertain the factors responsible for the poor results in these patients (Table XVIII).

Deaths

Nine deaths occurred in the group of 75 patients—four at operation or soon after, three within six months, and two within a year. The factors which may have contributed have been analysed in Table XIX. Consideration of both the poor results and deaths (15 patients) shows that multiple factors have been responsible.

In 10 patients technical difficulties at operation were responsible for failure. Mitral incompetence was produced or increased in four patients, a heavily calcified valve could not be split in three, ventricular fibrillation occurred in two, and infective endocarditis secondary to an auricular stitch abscess in one. In two patients a tear in the auricle also occurred. In one other patient failure to diagnose severe mitral incompetence before operation led to disaster, but four patients remain in whom reasons for failure are less clear cut. These reasons include coronary artery disease (later proved in one, and suspected in another), and persistent congestive cardiac failure before operation, which suggested irreversible myocardial and/or pulmonary vascular disease. In one of these patients a good split was thought to have been obtained despite heavy calcification, but necropsy showed that one of the cusps rather than the commissure had been torn.

Addendum

Since completing this survey, two further patients have deteriorated. One, a man with a heavily calcified valve, upon whom valvotomy was performed because of repeated attacks of paroxysmal dyspnoea, and who, despite a poor split, had a fair clinical result and was able to return to work, became rapidly worse 15 months after operation. On admission to hospital he was found still to have radiological evidence of severe pulmonary vascular disease: he died suddenly from pulmonary oedema. At necropsy the mitral valve was stenosed and extensively calcified (Fig. F).

FIG. F.—Case G. H. Necropsy specimen showing heavily calcified mitral valve.

The other patient, who had greatly improved in spite of a poor split, complained of increasing dyspnoea two years after operation. Clinical and radiological examination suggested severe pulmonary hypertension, and the cardiogram showed an increase in right ventricular hypertrophy, after an initial improvement (Figs. G, H, and I). Cardiac catheterization performed two and a half years after operation revealed a slight fall in pulmonary artery pressure, but pulmonary hypertension was still severe. Both these

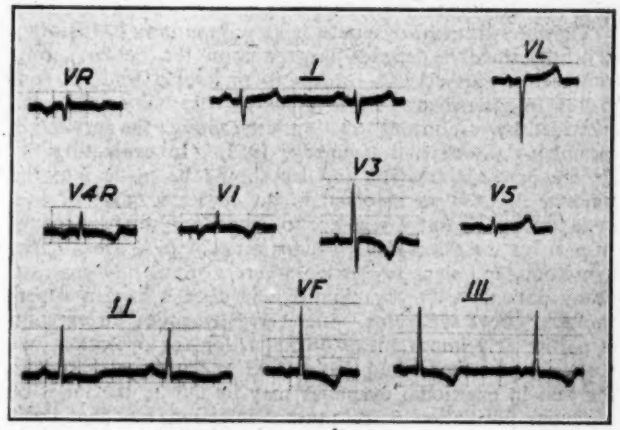

FIG. G.—Case M. C. Cardiogram showing severe (Grade II) right ventricular hypertrophy before operation.

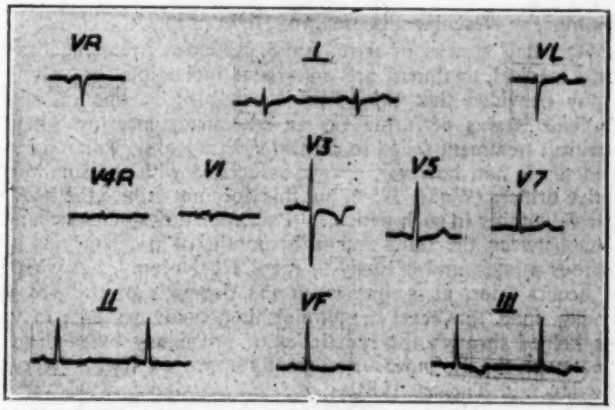

FIG. H.—Case M. C. Cardiogram 1½ years after operation, showing reduction in right ventricular hypertrophy.

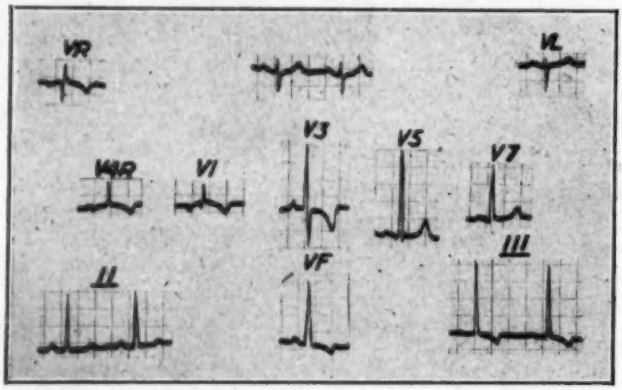

FIG. I.—Case M. C. Cardiogram 2½ years after operation, showing return of Grade II right ventricular hypertrophy.

patients had severe pulmonary hypertension, assessed both by catheterization and radiologically, prior to operation. A third patient (E. G.) listed as a poor result because of progressive congestive failure caused by mitral incompetence produced at operation, came to necropsy: the posterior cusp of the mitral valve had been torn through, leaving gross incompetence.

DISCUSSION

Diagnosis of Mitral Valve Disease.—Three important questions must be answered about any patient with mitral disease. (1) Is the mitral valve disease severe and disabling or threatening life? (2) Is the valve amenable to surgery? (3) Will the patient benefit from operation?

The most important symptoms to be considered when valvotomy is contemplated are dyspnoea on exertion, paroxysmal dyspnoea, and the effects of systemic embolism.

The assessment of dyspnoea is very important, but is often difficult, since it depends largely upon the patient's own statements. Associated bronchitis may also lead to confusion in assessment. Little practical help has so far been provided by respiratory function tests, though the results are promising (Stock and Kennedy, 1953). In evaluating the degree of dyspnoea, full inquiry should be made into the amount of exertion involved in the patient's mode of life. A sedentary life and reluctance to admit to dyspnoea account in part for the discrepancies sometimes found between slight symptoms and signs suggesting severe disease. By contrast, many patients with organic valvular disease have a superimposed effort syndrome. Increasing dyspnoea on exertion is particularly important as an indication for operation, but it should be remembered that attacks of dyspnoea or sudden increase in exertional dyspnoea may be due to the onset of auricular fibrillation or respiratory infection, and that these can be quickly and adequately controlled by medical treatment. Pulmonary oedema is in our experience more often than not associated with severe pulmonary hypertension, pulmonary vascular disease, and tight stenosis.

Repeated attacks of paroxysmal dyspnoea occurring despite medical treatment are an urgent indication for valvotomy provided that the valve is suitable; in one of our patients it was performed as an emergency measure when medical treatment failed to control such attacks. Pulmonary oedema is not, however, always associated with the smallest valve orifices (Wood, 1954), but this does not reduce the need for valvotomy in such patients. Paroxysmal dyspnoea occurring between the third and fifth months of pregnancy is a serious matter, and is likely to require valvotomy, but when it occurs later, at a time when the demands of the pregnancy upon the heart are diminishing, many patients may be helped through the remainder of pregnancy by medical treatment, the dyspnoea being greatly improved after delivery (Logan and Turner, 1953).

We have not been impressed, in our series, by the frequency of repeated pulmonary embolism as a serious or lethal event in cases with a very high pulmonary vascular resistance (Wood, 1954). However, we believe that mitral valve disease is a cause of thrombotic occlusion of the large pulmonary arteries (Ball *et al.*, 1955).

Fatigue, associated with dyspnoea, has been a frequent finding, but we do not regard the former as an important lone symptom.

Our results confirm the findings of Bailey *et al.* (1952) that valvotomy and amputation of the left auricular appendage are successful in preventing recurrent systemic emboli. We have recommended operation for patients with *repeated* embolism (provided the valve is suitable), even if dyspnoea is slight, for it is well known (Daley *et al.*, 1951; Wilson and Greenwood, 1954) that the risk of further emboli increases with each embolic incident. But we have not recommended operation for any patient with a history of a single embolus in the absence of other symptoms.

When it has been determined that the patient has disabling symptoms due to mitral valve disease, it is necessary to know whether the valve is suitable for operation. We agree with Sellors *et al.* (1953) that mobility of the mitral valve is of paramount importance, because in our experience a mobile valve usually splits well and is rarely significantly incompetent. The signs of a mobile valve are a loud first sound in the mitral area and an easily recognized opening snap. Severe pulmonary hypertension may mask these signs. Heavy calcification almost invariably produces a rigid valve, so that the signs of mobility are absent (Wynn, 1953). However, signs of a mobile valve may occasionally be combined with radiological evidence of heavy calcification, and under these circumstances valvotomy may be undertaken with expectation of a good result, as was the case in one of our patients.

We have found the diagnosis of predominant mitral incompetence to be dependent upon multiple signs. These are: a blowing systolic murmur at the apex, conducted to the axilla and maximal in expiration; enlargement of the left ventricle (without any other obvious cause); and considerable enlargement of the left auricle. Although we have noted a soft first sound in other cases of incompetence, this has not been a notable finding in the 10 patients presented here who had significant stenosis in addition to incompetence. In our experience the presence of heavy calcification does not necessarily indicate incompetence.

When it has been established that the valve is mobile, and that there is no important incompetence, it is necessary to determine whether the mitral orifice is critically narrowed, which we have found to be the case when the diameter is 1.5 cm. or less. This was the finding in the vast majority of our patients in whom symptoms warranted valvotomy; and in over half of them the orifice was even less than 1 cm. We believe that the size of the orifice can be assessed by clinical and radiological means. There is a significant relation between the grade of dyspnoea and valve size; the majority of patients with Grade III dyspnoea had a mitral orifice of less than 1 cm.

Further information about valve size can be gained from an assessment of pulmonary hypertension, which usually bears an inverse relation to the size of the mitral valve orifice. In our experience the radiological changes have proved more helpful than clinical or cardiographic assessment, and this method of assessment avoids the hazards of catheter studies. Radiological evidence indicating significant pulmonary hypertension and vascular disease is reliable evidence of a critically stenosed valve.

However, it is likely that pulmonary vascular disease takes time to develop, and lags behind critical valve-narrowing. This may be the reason why radiological changes were absent in 14 of our subjects who had significant symptoms and a critically narrowed valve.

When there are no radiological changes of pulmonary vascular disease, operation should not be advised unless there is clinical or other evidence of critical narrowing of the mitral valve to support the symptoms.

More rarely, signs of tight stenosis and serious pulmonary vascular disease may occur in the absence of any remarkable symptoms. This latter paradox might be explained by the alleged " protective " influence of a very high pulmonary arteriolar resistance upon the pulmonary capillaries (Lewis *et al.*, 1952 ; Wood, 1954).

The degree of left auricular enlargement is usually slight or moderate in patients with a critically narrowed mitral orifice and pulmonary hypertension, very large or aneurysmal auricles being nearly always associated with severe mitral incompetence. Nevertheless, aneurysmal enlargement may accompany pure or predominant stenosis, as was reported by Venner (1954) and was found in two of our own patients (Plate, Fig. 1).

Optimum Time for Valvotomy

It is difficult to establish the optimum time for valvotomy, but the results in 41 patients at one year after operation were appreciably better in those with Grade II than in those with Grade III dyspnoea, and this suggests that operation should be advised before the patient has developed Grade III dyspnoea. But dyspnoea was progressive in most of our patients, and we consider that non-progressive Grade II dyspnoea in the absence of signs of pulmonary hypertension is an indication for observation rather than immediate valvotomy, for such patients may have a valve which is not critically narrowed, have little or no pulmonary vascular disease, and may not deteriorate for a long period. It is likely that in two of our patients who had larger valves than we expected, operation could safely have been avoided.

Results of Mitral Valvotomy

The overall results agree in outline with those published previously (Baker *et al.*, 1952 ; Sellors *et al.*, 1953 ; Logan and Turner, 1953 ; Douglas and Hill, 1954 ; Wood, 1954), and indicate that in general the operation is satisfactory and worth while. Assessment of patients post-operatively has depended largely upon improvement in effort tolerance and in symptoms such as bronchitis, paroxysmal dyspnoea, and haemoptysis, all of which disappear or are greatly reduced after a successful operation. There has been little objective change, only a minority of our good-result patients showing any diminution in the signs of mitral stenosis or of pulmonary hypertension, reduction in heart size, or improvement in the cardiograph. However, gain in weight and increase in pulse volume and in the temperature of the extremities have been noted in some cases.

The absence of further serious systemic emboli after valvotomy is gratifying. The absence of free clot in the auricle in the majority of the patients who have had emboli gives support to the view that thrombus is rapidly organized, or rapidly detached and thrown off into the general circulation (Wood, 1954). There is certainly no reason to think that the risk of embolism during valvotomy is increased if the patient has previously suffered from embolic phenomena.

The duration of improvement after valvotomy is difficult to predict, but our results suggest that patients continue to improve up to one year, after which some deteriorate but few are likely to improve further.

Although good results were obtained in the majority of cases, it is important to examine in detail the poor results, the deaths, and the risks of the operation. Our results show that technical factors at operation were responsible for failure in 10 of 15 patients who died or had a poor result. Of these, the most important were the production of mitral incompetence, auricular tears, and failure to split a heavily calcified valve. The last hazard may be avoided if patients who have heavy valve calcification together with signs of a rigid valve or mitral incompetence are judged unsuitable for operation, except as a desperate measure. In two such patients substantial improvement was obtained for periods of one and two years respectively, despite a poor split, but the additional hazards and the uncertainty of the prognosis were clearly understood.

There seems to be no way of predicting whether the auricle will tear (and if so, whether further complications will follow, as in two of our patients) or whether severe incompetence will be produced. These two hazards must be included in the basic risks of the operation, and are adequate reason (even if there were no others) for the exercise of care and judgment in advising valvotomy. A further recognized hazard is the occurrence of a disabling or fatal systemic embolism. We have not encountered this serious complication, but it is clear that it may be of considerable importance (Sellors *et al.*, 1953 ; Wood, 1954).

Failure of the operation in four patients could not be ascribed to any single circumstance, and we believe that multiple factors—a poor split, production of incompetence, coronary artery disease and chronic congestive failure—all contributed to the result. We consider that chronic congestive heart failure which cannot be controlled by medical treatment is a serious bar to successful valvotomy, and suggests irreversible myocardial and/or pulmonary vascular changes. Such patients are probably past the stage at which surgical treatment can help them.

Apart from the technical hazards of valvotomy, there are certain other possible disadvantages to the patient which deserve mention. The incidence of the onset of auricular fibrillation after valvotomy is approximately 30% in our series, which agrees with the experience of Sellors *et al.* (1953). Although the majority of these patients can be restored to normal rhythm, many revert to fibrillation, and operation may be said to have induced fibrillation in 17 of our cases. This may merely be anticipating the inevitable course of events in a patient with mitral stenosis, but it is a disadvantage (Hansen *et al.*, 1952). The failure of valvotomy to influence established fibrillation suggests that the narrowed mitral valve is by this time merely part of a generalized cardio-pulmonary disease, all aspects of which are unlikely to be cured by merely increasing the size of the mitral orifice.

Absolute Contraindications to Mitral Valvotomy

The following conditions are an absolute contraindication to mitral valvotomy: severe mitral incompetence, intractable congestive failure, predominant aortic valve disease, and active rheumatic fever. However, where mitral stenosis and aortic stenosis are associated, surgical techniques now permit combined mitral and aortic valvotomies.

Special Problems of Mitral Valve Disease

(a) Active Rheumatic Carditis

There is no doubt that the effects of narrowing of the mitral valve are extremely important, but the part played by persistent and recurrent carditis in causing myocardial damage or increasing the stenosis is not yet known. We accept the general view that valvotomy is contraindicated in the presence of obvious acute or subacute rheumatism, but we have had great difficulty in assessing the importance of such isolated findings as persistent tachycardia, recurrent sore throats, persistently raised E.S.R., increased P–R interval on the cardiograph, and paroxysmal arrhythmias, as an indication of active carditis. We have found the antistreptolysin titre of little diagnostic value. There has been no correlation between the auricular biopsy, the post-operative course, and the clinical result.

None of the fatal or poor results could be attributed to active rheumatic carditis. It is surprising that patients whose auricular biopsy showed evidence of considerable rheumatic activity ran a similar course after operation to patients without such changes, particularly in view of McKeown's (1953) findings that the left auricular biopsy mirrors changes in the ventricular myocardium. We do not agree with Rothschild *et al.* (1934) that most patients with rheumatic heart disease die from active myocardial disease and few from the mechanical effects of diseased valves, but we are equally sure that the myocardium should not be neglected when evaluating the prognosis and the suitability of patients for valvotomy.

(b) Re-stenosis of the Mitral Valve

Magarey (1951) has suggested that re-stenosis can occur, and Wood (1954) has reported it in 5% of his cases. But Glover *et al.* (1955) consider that re-stenosis is very unlikely if a satisfactory split has been obtained. It has not been suspected in any of our patients in whom a good split has been achieved, but the time interval is as yet comparatively short. However, in three patients in whom a poor split was achieved we have reason to believe that re-stenosis had led to recurrence of dyspnoea. It has not been possible to diagnose this by any particular method, but when a patient has had a period of relief from symptoms following operation and then the symptoms return, it would seem justifiable to suspect this, although there are other possible factors, such as persistent pulmonary vascular disease.

(c) Pulmonary Vascular Changes

It is usually considered (Holling, 1952) that pulmonary arteriolar constriction is a reversible process, and indeed the vascular resistance has been shown to fall after valvotomy (Baker *et al.*, 1952; Werkö *et al.*, 1952).

Although narrowing of the small pulmonary arteries which has been demonstrated in life (Goodwin *et al.*, 1952) has been frequently absent at necropsy, in some cases organic occlusive changes have been demonstrated (Parker and Weiss, 1936; Larrabee *et al.*, 1949; Henry, 1952; Harrison, 1953; Steiner and Goodwin, 1954). There is considerable evidence to support the contention that the narrowing is initially a functional one (Bayliss *et al.*, 1950; Davies *et al.*, 1954), but the possibility is not excluded that this may persist after valvotomy. Harrison (1954) has found hypertrophy of the muscular coats of the pulmonary arterioles at necropsy in patients with mitral stenosis—changes which would be consistent with persistent pulmonary hypertension.

It is somewhat perturbing to note that radiological evidence of pulmonary hypertension has not regressed in two-thirds of our cases with good or fair results, suggesting that pulmonary vascular changes remain despite symptomatic improvement. We have not subjected the patients with good results to cardiac catheterization post-operatively, but the findings of Wade *et al.* (1954), who showed that the mean pulmonary artery pressures did not fall post-operatively in four out of eight patients with good results, support this suggestion.

Although persistent pulmonary hypertension assessed radiologically has not interfered with a good symptomatic result in the majority of our patients, we cannot exclude it as a factor of importance, especially in those who showed initial improvement but later deteriorated. However, we have noted an increase in the changes in only one patient, so that it is possible that valvotomy can halt the progress of vascular disease.

The Future of Mitral Valvotomy

In the most suitable type of patient we estimate that there is an irreducible failure rate of 5% with the present type of operation. In less suitable cases, therefore, the risks are considerably higher, but may be worth taking in special circumstances.

A more detailed knowledge of the natural history of mitral valve disease than is now available would be very desirable. Wood (1954) has shown that deterioration in symptoms can be rapid, the average period from the onset to total incapacity being approximately seven years in his series. However, mitral stenosis is not inevitably a progressive disease (Wilson and Greenwood, 1954).

But we believe that when a patient develops progressive and severe dyspnoea which is not attributable to temporary complications that can be controlled, such as excessive physical exertion, pregnancy, or the onset of uncontrolled auricular fibrillation, deterioration is likely to be progressive.

We have been unable to detect any objective evidence of improvement in two-thirds of the cases showing good results, which throws a heavy burden upon the subjective assessment of improvement and accentuates the need for a reliable test of exercise tolerance. We have been fully aware that diminution of dyspnoea may sometimes be the result of factors other than improvement in cardiac function. The psychogenic effects upon the patient of a serious operation, together with a prolonged period of rest in bed, must not be neglected. Soloff and Zatuchni (1954) quote the remarkable symptomatic improvement in four patients who had a thoracotomy but no valvotomy, reported by Varco and Baronofsky, and add one case of their own. Mitral valvotomy is undoubtedly valuable and sometimes life-saving, and should certainly be carefully considered in any patient with mitral disease who has important symptoms. However, the possible disadvantages and the operative mortality must be carefully weighed against the patient's prognosis and the natural history of the disease.

SUMMARY

The pre-operative and operative findings in 75 patients with mitral stenosis are presented, and the results of mitral valvotomy are assessed in 56 patients who have been followed for six months to three years. Special attention is paid to the progress of patients during the follow-up period.

Comparison of the degree of dyspnoea, degree of pulmonary hypertension, and degree of pulmonary vascular disease, with the valve orifice found at operation, suggested that critical mitral stenosis may be expected if there is severe dyspnoea and severe pulmonary hypertension (best assessed radiologically).

If auscultation revealed evidence of a mobile valve and no incompetence, a good split could be predicted. Heavy calcification and signs suggesting a rigid valve militated against a successful valvotomy.

The majority of patients were greatly improved symptomatically after operation, but in only one-third of those with good subjective results was there any objective evidence of improvement. Pulmonary vascular disease, assessed radiologically, did not alter in two-thirds of patients with a good result—suggesting that valvotomy, although it may halt the changes, may fail to cause any reversion.

Special attention has been paid to all the pre-operative factors which might have influenced the result: there was no constant trend, except that all the patients with Grade II dyspnoea had a good result at one year, as compared with a good result in only 50% of those with Grade III dyspnoea.

Analysis of the poor results and deaths (15%) showed that operative factors were responsible in the majority: such as the production of severe mitral incompetence, tearing of the auricle, ventricular fibrillation, and failure to split a heavily calcified valve. In the remainder, age, coronary artery disease, and chronic unmodified congestive heart failure may have been responsible for failure of the operation.

The results of the operation are discussed in the light of the natural history of the disease and the operative risks and mortality. Factors which may influence the result but which are difficult or impossible to assess, such as active rheumatic carditis, re-stenosis, and pulmonary vascular disease, have been specially considered.

We wish to thank all those who have kindly referred patients to us, especially the physicians of Hammersmith Hospital, and particularly Professor J. McMichael. We are also indebted to the many house-surgeons and registrars who have helped greatly with the care of patients and the collecting of notes. We are especially grateful to Sisters Anderson and Pryor, whose devoted nursing care contributed substantially to the results. Mr. D. Simmonds

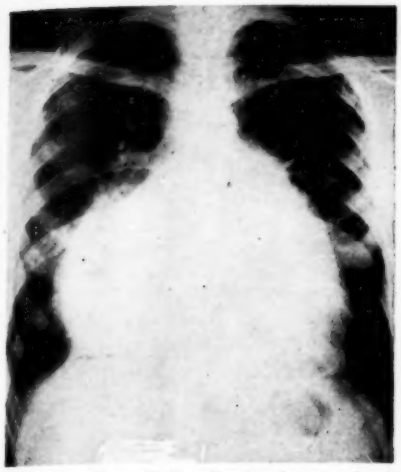

FIG. 1.—Case T. S. Predominant mitral stenosis. Six-foot (1.8-m.) postero-anterior radiograph, to show aneurysmal left auricle, also enlargement of the main pulmonary arteries. Fine horizontal striations (Kerley's lines) at right costo-phrenic angle.

FIG. 2.—Case J. H. Six-foot (1.8-m.) postero-anterior radiograph showing considerable cardiac enlargement before operation.

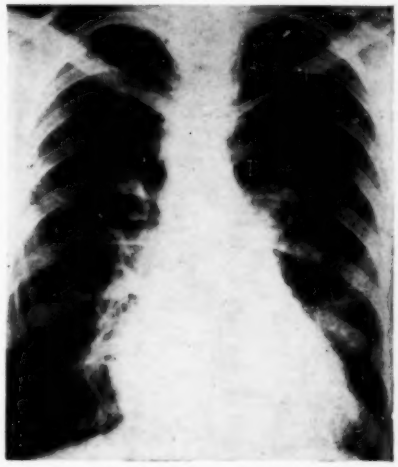

FIG. 3.—Case J. H. Radiograph 15 months after operation, showing reduction in size of the heart.

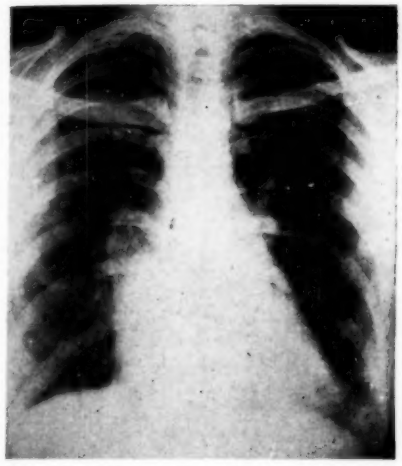

FIG. 4.—Case J. S. Six-foot (1.8-m.) postero-anterior radiograph showing normal right auricle before operation.

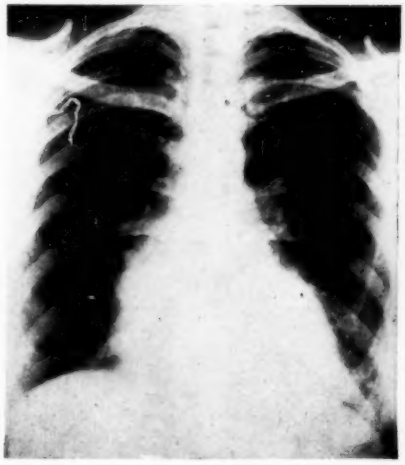

FIG. 5.—Case J. S. Radiograph showing enlargement of the right auricle two years after operation.

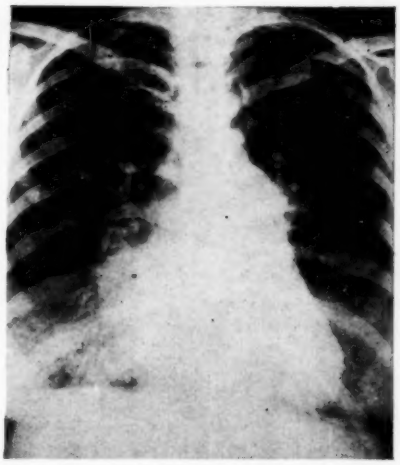

FIG. 6.—Case V. T. Six-foot (1.8-m.) postero-anterior radiograph showing severe (Grade II) pulmonary hypertension before operation.

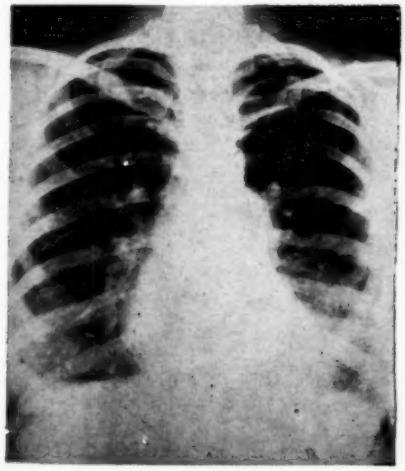

FIG. 7.—Case V. T. Radiograph 18 months after operation, showing reduction to moderate (Grade I) changes.

FIG. 8.—Case A. T. Right lower zone of right lung, showing severe vascular changes and prominent Kerley's lines.

FIG. 9.—Case A. T. Showing disappearance of Kerley's lines and improvement in vascular pattern after operation.

FIG. 1.—Normal appearances.

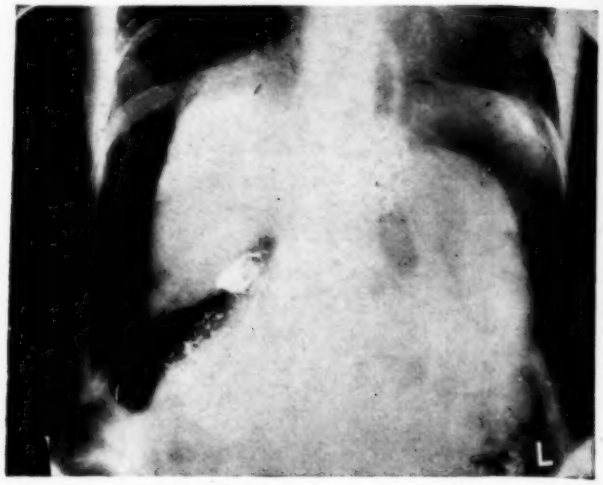

FIG. 2.—Alcoholic cirrhosis. Liver small with "hobnail" surface. Spleen probably normal.

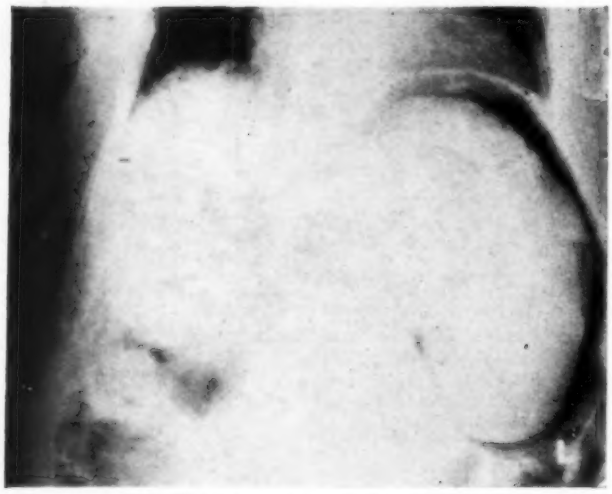

FIG. 3.—Biliary cirrhosis. Liver small and adherent to diaphragm. Spleen much enlarged.

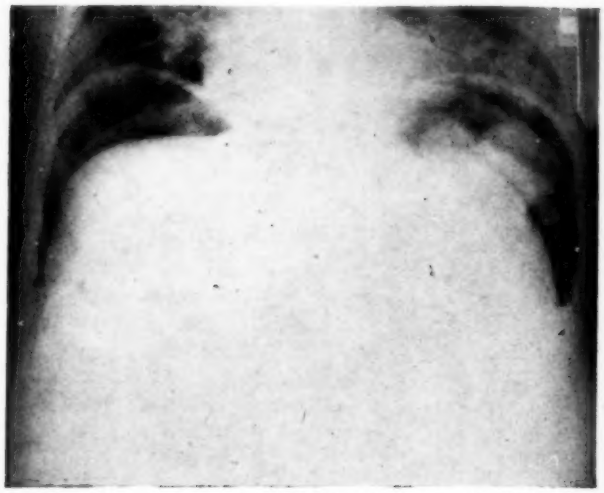

FIG. 4.—Secondary neoplastic deposits below the left diaphragm. Liver and spleen normal.

FIG. 5.—Retroperitoneal neoplasm with displacement of spleen. Liver normal. Lower pole of spleen set low. No air above the spleen, because of a tumour subsequently found at operation.

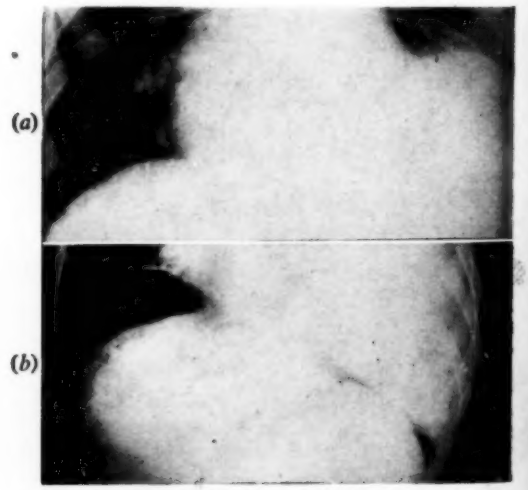

FIG. 6.—Pleural effusion mimicking high left diaphragm. (*a*) Plain *x*-ray film. (*b*) Film after pneumoperitoneum showing diaphragm to be low.

kindly prepared the diagrams, and we are pleased to thank Mr. T. W. P. Knowlden, of the Department of Medical Photography, for the photographs.

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A study of the effect of cultural conditions on human fertility in non-industrial or transitional societies, initiated by Unesco, was undertaken by Professor Frank Lorimer, of the American University, in 1951. *Culture and Human Fertility*, price 25s., is the Unesco publication reporting his findings. The first half of the book, by Professor Lorimer himself, is devoted to general theory. In it he states that variations in birth rate "are more powerfully influenced by social and psychological factors" than by conditions of climate or nutrition. All societies, however, were found to practise some method of population control, those in the Pacific being more conscious of the need to adapt numbers to resources than the African. The chief cultural factor influencing fertility seems to be the kinship system: this can be unilateral—that is, either matrilineal or patrilineal—a mixture of both, or, as in Western civilization, have the couple, not the clan, as family nucleus. In both unilateral systems children are welcomed as strengthening the group. Conquest was found to have an adverse effect on the birth rate. The second half of the book, compiled by Professor Lorimer's colleagues, is a record of field-work in demographically interesting areas. The Ashanti were studied as a matrilineal society, the Buganda as a group where tribal authority is losing ground, and Brazil because the population has risen in about a century from 7 to 52 million. Inhabitants were asked about the age of menarche and first marriage, and figures for reproductive rates and infant mortality. Their attitude to pregnancy, extra-marital relations, divorce, and population control was studied.

DIAGNOSTIC PNEUMOPERITONEUM

BY

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AND

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[WITH SPECIAL PLATE]

Although there are a number of references to the usefulness of pneumoperitoneum for visualizing various abdominal organs, the procedure has not come into general diagnostic use, as is clear from the scant mention it receives in standard textbooks of diagnostic radiology. We have recently been using this procedure as an aid to radiological diagnosis of abdominal disease, with particular reference to the gross morbid anatomy of the liver and spleen. Our observations are still limited in number, but we are satisfied that excellent radiographs of these and other abdominal organs can be obtained with the help of this technique, and we believe that it has a useful place among diagnostic methods.

We now present illustrative examples of the findings obtained in a group of patients studied by this method. Although we have so far been particularly interested in the liver and spleen, other abdominal organs can be studied, as will be evident from some of the illustrations we have chosen.

Methods

Induction of Pneumoperitoneum

We have induced pneumoperitoneum in one or other of two ways, according to the particular patient.

In Patients with Ascites.—In patients with ascites who are subjected to paracentesis, air can immediately be introduced into the peritoneal cavity through the cannula used for draining off the ascitic fluid. This procedure can be carried out with ease. The fact that ascitic fluid is flowing freely through the cannula ensures that its tip is correctly located within the peritoneal cavity. When enough ascitic fluid has been drained off to leave ample space for the air to be introduced, the cannula is connected to an appropriate instrument and air injected. We have used the Maxwell pneumothorax apparatus as being convenient for delivering a known quantity of air, but it is evident that a simple three-way syringe would be adequate. In cases of ascites which come to paracentesis there is usually a large amount of fluid, so that a partial air replacement (1,500–2,000 ml.) can be carried out without causing discomfort, while ensuring that plenty of air is present to facilitate radiological examination. In our opinion the risk of this procedure is negligible. If one listens to the abdomen with a stethoscope while the air is being introduced, the air can be heard bubbling through the ascitic fluid like a burst of machine-gun fire. Alternatively a hand placed on the abdominal wall feels the tactile equivalent of the same phenomenon. These signs confirm that the air is being correctly introduced.

In Patients without Ascites.—In these cases a formal induction of pneumoperitoneum must be carried out on the lines now widely used by chest physicians who employ this method as a form of therapy. Good descriptions of the technique are given in most standard textbooks of pulmonary tuberculosis, such as those by Pagel *et al.* (1953) and by Sellors and Livingstone (1952). We have used a Saugmann refill needle inserted after local analgesia into the abdominal cavity at the lateral border of the left rectus abdominis muscle. If the spleen is enlarged the insertion should be made at or below the level of the umbilicus. We have

found that about 1,000 ml. of air is necessary to ensure excellent radiographic views of the liver and spleen, although less complete studies can be made with 500 ml. It has been our practice to induce pneumoperitoneum with about 500 ml. of air on the day before the *x*-ray examination. On the day of examination the patient is first examined by screening in the erect position to confirm that the air has been correctly introduced, and a refill of another 500 ml. is performed on the *x*-ray table before proceeding to the full examination described below. In this way the patient is subjected to the minimum amount of interference.

The formal induction of a pneumoperitoneum demands more skill and judgment than the partial air replacement of ascitic fluid, but it is neither difficult nor dangerous if carried out with proper precautions.

Radiological Techniques

Position of Patient.—The *x*-ray examination is carried out with the patient on a tilting table. The first step, which is taken whenever the patient's condition permits, consists of a screen examination of the chest and abdomen with the patient erect. With change in the patient's position, free gas in the peritoneal cavity travels readily within that cavity, tending always to collect in the part which is uppermost. Examination with the patient in an upright position therefore shows the free air under the diaphragm—a view familiar in chest radiographs after therapeutic pneumoperitoneum. In the absence of any condition which would cause unusual distribution of the air, the amounts seen on the two sides are approximately equal.

Next the patient is brought into the horizontal prone position by lowering the table while he faces it. Some padding between the chest and thighs may be required for the patient's comfort, particularly if he has ascites. In normal subjects, and also in most cases with disease, in this position the liver and spleen are well outlined by air so that the profile of much of the liver and most of the spleen can be seen. This is the position above all which gives a general view of the size, surface, and relations of these two organs. A single 15 by 12 in. (38 by 30 cm.) film of this view includes the whole of both organs unless there is very great enlargement.

It must be emphasized that the patient is face downwards for this part of the examination. If a patient with pneumoperitoneum is examined in the supine position the air collects immediately under the anterior abdominal wall and fails to outline any of the abdominal viscera. This fact may explain why pneumoperitoneum has been little used in diagnosis.

If either the liver or spleen is poorly outlined by air on the first view obtained in the horizontal prone position, advantage may be taken of the free movement of air to induce more to surround each organ in turn. The patient is turned briefly on to one side (still remaining horizontal) with the poorly outlined organ upwards. On returning the patient to the horizontal prone position the air is found almost entirely on the side which has been uppermost. The vertebral column evidently juts far enough into the abdominal cavity to create separate air compartments when the patient is prone.

Supplementary views may also be taken with the patient lying on one or other side and with the *x*-ray beam used horizontally.

Radiographic Technique.—It is easy to obtain good-quality radiographs of patients with pneumoperitoneum, and a variety of techniques are applicable. However, it may be of value to record some details of the methods we have used.

Radiographs of the patient in the horizontal prone position are taken with an over-couch tube at a distance of 110 cm. A Potter–Bucky diaphragm is usually employed, but pictures of good quality can be obtained without it if the patient is not stout. When a horizontal beam is used, exposures are made with the tube at a distance of 100 cm. and a cassette incorporating a fixed grid.

As an example, in a man of average build the exposure factors are as follows :

Position of Patient	Grid	Distance	kVp	mA secs.	Films
Horizontal prone	Potter–Bucky	110 cm.	86	24	Ilford standard
,, ,,	None	110 ,,	70	12	,, ,,
Lateral, with horizontal beam ..	Stationary	100 ,,	82	20	,, ,,

Results

Normal Appearances

The use of pneumoperitoneum as a therapeutic measure in pulmonary tuberculosis provides a source of material for studying the range of normal appearances of abdominal organs, provided that tuberculous patients in good general condition and without evidence of abdominal disease are selected.

Fig. 1 on the Special Plate shows the radiological appearances of a typical tuberculous subject, whom we regard as "normal" in the present context. This film was taken in the horizontal prone position, which, as mentioned above under "Radiological Techniques," is the one most generally useful for a view of the outlines of the liver and spleen. The right lobe of the liver is well outlined and its characteristic shape and smooth surface are well shown. Overlapping the inner half of the right lobe of the liver, the lateral border of the right kidney shows up sharply. On the left side the spleen is well revealed, both upper and lower poles being clearly outlined. The left kidney is less well seen than the right, and its border is not precisely shown—a finding which is usual. The fundus of the stomach with its small contained air-bubble can be seen overlapping the upper pole of the spleen.

Alcoholic Cirrhosis

The patient from whom the radiograph shown in Fig. 2 was taken, a woman aged 68, was admitted to the Radcliffe Infirmary on September 24, 1954, suffering from ascites. She had worked as a licensed victualler for many years, but had retired some years ago and was living a quiet life looking after her aged mother. She had a liking for bottled stout, and when feeling depressed sought solace in "one or two gins."

On examination there was found to be gross ascites. A number of spider naevi were present on the skin. The blood count was normal. The urine contained a small amount of protein. The blood urea level was normal (25 mg. per 100 ml.), so also was that of total plasma proteins (6.8 g. per 100 ml.), but the albumin component was low (3 g. per 100 ml.). The plasma bilirubin level was slightly raised (1.9 mg. per 100 ml.), but flocculation tests of liver function (thymol turbidity and colloidal gold) were negative.

A paracentesis abdominis was performed with removal of 4 litres of ascitic fluid which was clear, straw-coloured, and lymphocytic. Paracentesis was carried out twice more during the next ten days, and on the last occasion 2,000 ml. of air was introduced through the paracentesis cannula in the manner described earlier and the patient examined radiologically. In view of the large amounts of ascitic fluid withdrawn, this amount of air was not judged to be excessive.

The radiograph (Plate, Fig. 2) shows a liver greatly reduced in size. The whole surface of the organ is closely studded with small nodules, giving rise to the classical appearance of "hobnail liver" familiar in post-mortem studies of these subjects. The spleen does not appear to be significantly enlarged. Some barium is present in the stomach and small intestine, but is not relevant to the present findings.

Biliary Cirrhosis

The radiograph in Fig. 3 is from a woman of 73 admitted to the Cowley Road Hospital. In 1944 her gall-bladder was removed because of cholelithiasis, and two years later her common bile duct had been explored. Subsequently biliary cirrhosis developed. In 1949 she again had a laparotomy for exploration of the common bile duct, but no gall-

stones were found. Recently she had suffered from liver failure, but at the time of our examination she was relatively well. There was no jaundice and no ascites, and her general state of nutrition was good. The spleen was much enlarged.

Formal induction of a pneumoperitoneum was carried out, and the radiograph shows the appearance of the liver and spleen. The liver is very small. No air would travel between it and the diaphragm, which we take to be a sign of extensive adhesions between the two. The inferior border of the liver appears coarsely irregular; we cannot decide whether this is due to extensive scarring of the liver or to adhesions. The spleen is greatly enlarged, with a smooth surface.

Peritoneal Metastases of Neoplasm

A man aged 46 was admitted to the Radcliffe Infirmary in May, 1954, because of haematemesis following a one-year history of dyspepsia. After medical treatment he made an uneventful recovery from the haematemesis, but radiological examination revealed a carcinoma of the stomach. At operation a large fungating tumour was found and a number of lymph nodes showed evidence of malignant involvement. A palliative partial gastrectomy was performed. Thereafter he was well until November, 1954, when bronchitis with vomiting developed and he was readmitted to the Radcliffe Infirmary suffering from ascites. The ascitic fluid was partially replaced by air and he was examined radiologically. The liver and spleen appeared to be normal, but there was evidence of multiple peritoneal metastases. In Fig. 4 we have selected a film which shows some of these located immediately above the spleen; other views not reproduced here showed that these deposits were below the diaphragm. Both leaves of the diaphragm are thickened and their inferior surfaces appear irregular in places.

The patient later died and was examined post mortem, when extensive peritoneal deposits were found. The spleen was normal, as also was the liver apart from one solitary nodule, 1 cm. in diameter, probably a secondary deposit.

Retroperitoneal Tumour Displacing the Spleen

A man aged 49 was transferred to the Radcliffe Infirmary from another hospital in December, 1954, with a six-months history of pyrexia and pain in the left side of the abdomen. In the previous September a chest radiograph had shown a left pleural effusion and aspiration had yielded a pleomorphic fluid with no malignant cells seen. In November, 1954, a mass was felt below the left costal margin which was thought to be the spleen. Hodgkin's disease was regarded as a likely diagnosis.

There was disagreement on whether the palpable mass was a spleen or not. Formal induction of a pneumoperitoneum was carried out and some of the subsequent radiological findings are shown on the Plate (Fig. 5). The liver appears normal. The lower border of the mass is clearly the spleen. No air would travel above this organ. We could not decide why the air failed to pass around the spleen to appear beneath the left diaphragm. At operation a large retroperitoneal tumour, probably a reticulosarcoma, was found in the left upper abdomen, pushing down the spleen and itself occupying the subdiaphragmatic space.

Pleural Effusion Mimicking High Left Diaphragm

The patient with whom Fig. 6 on the Special Plate is concerned was a young man of 23 with a long history of lymphatic derangement. Some puffiness of the face was noticed at 2½ years of age. Later he developed gross swelling of the legs and scrotum with the characteristics of a lymphatic oedema. However, he was generally well and worked as a builder's labourer. On seeking to change his occupation he was subjected to *x*-ray examination of the chest, and this showed an opacity in the left thorax which required investigation. There were physical signs suggesting a pleural effusion, and paracentesis thoracis yielded a chylous fluid. However, the appearance of the chest radiographs at that time (Fig. 6*a*) gave rise to doubt whether a pleural effusion was the whole explanation, particularly as some clinicians thought that they could palpate the spleen. Extensive *x*-ray investigations with the help of pneumothorax failed to settle the issue, and most of the radiologists concerned were of the opinion that the left diaphragm was raised. Formal induction of a pneumoperitoneum permitted an exact radiological assessment. Fig. 6*b* shows a low left diaphragm with a small, normal spleen lying beneath it.

Discussion

For about 40 years pneumoperitoneum has been used as an aid to radiological diagnosis, but it has not become generally accepted in Britain and we have been unable to find any British reference to its systematic use for the study of diseases of the liver and spleen. It was only after we had discovered the importance of the horizontal prone position when taking radiographs of the liver and spleen that we found this position already advocated in an article from Algeria by Aubry and others (1954). We therefore claim no originality in the radiological method, but are sufficiently convinced of its usefulness to recommend its more widespread adoption.

No diagnostic method should be recommended without some appraisal of the risks involved. In cases in which there is ascites we believe that the additional risk of introducing some air into the peritoneal cavity during paracentesis abdominis is negligible so long as attention is paid to the physical signs described in the relevant section above. The liver and spleen are frequently abnormal in patients with ascites; peritoneal deposits may be revealed by pneumoperitoneum, as exemplified in Fig. 4; and neoplasms of other abdominal organs, such as the ovaries, may likewise be demonstrated. For these reasons we now believe than any patient who suffers from ascites the underlying cause of which is not apparent should be studied by this method. With respect to a formal induction of pneumoperitoneum in patients without ascites, the method has been so extensively used as a therapy for pulmonary tuberculosis that fairly precise estimates of its dangers are available. Although a large number of different complications have been described (Stein, 1951) they occur but seldom, and serious complications are rare. In most patients the induction is painless and does not give rise to subsequent discomfort. In some patients, however, the procedure is followed by a tight feeling in the upper abdomen or pain in the shoulder tip. These symptoms can be relieved by keeping the patient supine for a few hours. The serious complications are air embolism, surgical emphysema of the anterior abdominal wall, mediastinal emphysema, spontaneous pneumothorax, and perforation of a viscus. Correct attention to the technique of induction will minimize the risk of these. Fatal complications are rare. For example, Simmonds (1946) reported only one death (due to air embolism) in the course of more than 13,000 air injections; and Trimble and others (1948) treated 407 tuberculous patients with pneumoperitoneum with only one death (also from air embolism) due to therapy.

Naturally some clinical judgment should be brought to bear on the selection of patients for diagnostic pneumoperitoneum. For example, it would be manifestly unwise to practise this procedure on a patient with congestive heart failure who has no respiratory reserve. However, provided such patients are excluded, we do not think that diagnostic pneumoperitoneum should be any more hazardous than when it is used for therapy. The risk involved seems to be low enough to permit our advocating its use in cases presenting diagnostic problems which pneumoperitoneum may help to solve.

Summary

Pneumoperitoneum is a diagnostic procedure which enables useful radiographic studies to be made of various abdominal organs. In particular, the liver and spleen can be clearly demonstrated by examining the patient in the horizontal prone position.

In patients suffering from ascites, pneumoperitoneum can be induced with great ease and negligible risk by performing partial air replacement at the time of paracentesis abdominis. This should be done in all patients with ascites in whom the underlying diagnosis is in doubt.

In patients without ascites, formal induction of a pneumoperitoneum is an easy procedure the risk of which is sufficiently low to justify its use as a diagnostic method.

Results with this method are presented with special reference to the liver and spleen. Its more widespread adoption is recommended.

We are grateful to Dr. R. R. Tilleard-Cole for clinical assistance, and are much indebted to Miss M. Bell, who carried out most of the radiography. We wish to thank our colleagues in the United Oxford Hospitals for referring patients to us.

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DUODENAL ULCER TREATED BY VAGOTOMY AND GASTRO-ENTEROSTOMY

RESULTS OF 100 CONSECUTIVE CASES

BY

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AND

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Many observers have recorded their results following vagotomy and gastro-enterostomy for duodenal ulceration, and experiences have varied. The purpose of this report is to add to these experiences the results obtained from a series of 100 consecutive cases of duodenal ulcer similarly treated. None of the patients were selected for this operation as opposed to any other, the only criterion for inclusion in the series being the need for surgical as opposed to medical treatment. In addition, between 1946 and 1948 one of us performed this operation on 45 occasions and it was the apparently satisfactory initial follow-up of these patients which prompted us to undertake the present series. However, a further incomplete check of these patients reveals that at least 9 (20%) have required further gastric surgery.

Material

Of the 100 patients 78 were men and 22 women. The youngest was 25, the oldest 77, with an average age of 45 years. The operations were performed by members of the surgical unit of St. Mary's Hospital, and these followed a standard pattern. This consisted of confirmation of the diagnosis by laparotomy, and a posterior gastro-enterostomy combined with resection of at least 1 in. (2.5 cm.) of the vagi and their branches after mobilizing and withdrawing into the abdomen the supradiaphragmatic portion of the oesophagus.

There was one almost immediate post-operative death associated with collapse and peripheral circulatory failure, probably due to a coronary thrombosis. The remaining 99 patients recovered and in due course were discharged to attend the follow-up clinic. Ten patients (10%) have defied all efforts to trace them recently enough for their inclusion in an evaluation of the results. Nevertheless an analysis of their progress, so far as it is known, is given later.

Eighty-nine patients (89%) have been followed up for varying periods, the average length of follow-up at the time of submitting this report being 29 months. Such a short follow-up probably fails to represent the final picture, but, as will be seen, the results are of such a nature as to warrant an early report. These patients were seen at increasingly long intervals unless their progress was unsatisfactory, when they were seen more frequently. Attention was paid to the patients' subjective state of health, their ability to undertake their normal work being considered important. Examination was primarily clinical, barium-meal studies and gastroscopy being undertaken only when the clinical findings warranted them. Fractional test meals and insulin test meals were not undertaken as a routine, because of the invalidity of achlorhydric results due to biliary regurgitation after a gastro-enterostomy.

Results

The results in these 89 patients have been classified thus: (1) Excellent; (2) good; (3) persistent post-operative syndromes with or without dyspepsia; (4) persistent dyspepsia alone, with no proved recurrence of ulceration; (5) recurrence of peptic ulceration; and (6) miscellaneous.

1. *Excellent.*—These results occurred in patients who subjectively and objectively were completely free of any dyspepsia or post-vagotomy and gastro-enterostomy syndromes from the immediate post-operative period. There were 33 such patients (37.1%). One died from cerebral haemorrhage two years after operation. Up to the time of his death he had had no recurrence of his symptoms, and at necropsy there was no evidence of further peptic ulceration.

2. *Good.*—Into this category fell patients who post-operatively had temporary disturbances, but which have now completely disappeared. There were nine such cases (10.1%). Six patients had temporary post-vagotomy and gastro-enterostomy syndromes, one patient had temporary dyspepsia, and two patients had both temporary post-operative syndromes and dyspepsia.

3. *Persistent Post-vagotomy and Gastro-enterostomy Syndromes With or Without Dyspepsia.*—Thirty patients (33.7%) still had persistent disturbances dating from the operation. Five of them also had dyspepsia, in one of which it was temporary and in four permanent. Whether associated with dyspepsia or not, 38 patients (42.7%) had post-vagotomy and gastro-enterostomy disturbances, of which 8 (9%) were temporary and 30 (33.7%) permanent. In two of the permanent cases some of the symptoms had disappeared, suggesting that ultimately they may fall into the temporary category.

Classification According to Severity

	Temporary	Permanent
Severe	—	6
Moderate	2	11
Mild	6	13

Of those suffering from permanent severe syndromes two felt worse for having the operation, two had to abandon their original jobs and undertake light work, and one has had to absent himself from work for a day or two every few weeks.

Classification According to Symptoms in Order of Prominence

Fullness after meals	22	Flatulence	4
Biliary regurgitation	8	Diarrhoea	4
Faintness related to meals	8	Easy fatigue	2
Nausea	7	Anorexia	2
Non-biliary regurgitation	5	Dysphagia	1

Some of the patients had multiple symptoms, and so the sum of the above figures exceeds the total of cases exhibiting post-operative syndromes.

4. *Persistent Dyspepsia Without Post-operative Syndromes and With no Proved Ulcer.*—There were five such patients (5.6%). These, together with the four cases of persistent dyspepsia occurring with post-vagotomy and gastro-enterostomy syndromes, are here analysed, making a total of nine (10.1%). In one case the symptoms were only those of "heartburn," but in the remainder they were similar to pre-operative symptoms, only in most cases milder. Six were mild, two were moderate, and one was severe. All these patients underwent barium studies apart from two of the mild cases, one being the patient with "heartburn" and the other a patient who has so far failed to attend for his radiological examination. In none of those examined was there any radiological evidence of ulcer recurrence. In view of this and the fact that all were able to work or attend to their household duties, their symptoms have been controlled by medical treatment and they remain under observation.

5. *Further Peptic Ulceration.*—There were 11 cases (12.4%)—eight have been proved at operation, and three have not undergone operation because one refused operation (gastric and duodenal ulceration), one was unfit for operation for other reasons (gastric and duodenal ulceration), and one was pregnant at the time this report was written and was awaiting operation (gastric ulceration). In all these three patients the diagnosis has been made not only on clinical grounds but on the unequivocal demonstration of an active ulcer crater radiologically.

Site of the Peptic Ulceration

Gastro-jejunal	Duodenal	Gastric	Gastric and Duodenal
6	1	1	3

Of these recurrences six occurred in men and five in women. The average duration before recurrence of symptoms was 16 months, the shortest being five months and the longest 26 months.

6. *Miscellaneous.*—One patient remained well for 22 months, when he had a severe melaena. Clinically and radiologically it was probable that he had a gastro-jejunal ulcer. Laparotomy failed to show such an ulcer, but following his gastrectomy, which was performed at this second operation, he has remained well up to date.

The Defaulters

Of the 10 defaulters there was no trace of five from almost immediately after discharge. Of the remaining five one was seen three months after operation with recurrence of pain, but refused treatment, and shortly afterwards left the country; one was seen one year later with recurrence of pain and vomiting, but he is a seaman and has since been untraceable; one was seen one year later and was well, apart from occasional pain and postprandial fullness; and two were seen one year later and were very well.

Summary of Results

Out of 100 cases of vagotomy and gastro-enterostomy for duodenal ulcer there was one post-operative death. Of the remaining 99 cases 10 defaulted and 89 were followed up. The results in these cases are as follows:

Category	No. of Cases	% of Cases Followed up
Excellent	33	37·1
Good	9	10·1
Persistent post-operative syndromes with or without dyspepsia	30	33·7
Persistent dyspepsia alone with unproved recurrence of ulceration	5	5·6
Proved recurrent ulceration	11	12·4
Miscellaneous	1	1·1

Conclusions

A recurrence rate of 12.4% is undeniably very high, particularly as the average duration of follow-up has been only 29 months: further continuation of the follow-up might produce an even higher percentage of recurrences. It is interesting to note that no fewer than eight patients in this series have undergone further operation for peptic ulceration.

Quite apart from the recurrences, there has been a remarkably high incidence of post-operative syndromes that have so far persisted. Admittedly many of these have been mild in nature, but in our experience vagotomy has little to offer in the search for an operation free of sequelae such as the syndromes which may follow partial gastrectomy. Indeed, in six cases the symptoms have been severe and have interfered with the patients' normal work.

Our inevitable conclusions are that vagotomy and gastro-enterostomy, in our hands, is an unsatisfactory operation for duodenal ulcer. If the operation demands for its greater success a highly specialized technique, we still consider it unsatisfactory: any operation for such a common disorder must stand or fall by the results obtainable in average hands.

We wish to thank Mr. H. H. G. Eastcott and Mr. D. L. P. Farley, who performed many of the operations included in this series and who have assisted us with the follow-up.

SPIROMETRY IN ASSESSMENT OF ANALGESIA AFTER ABDOMINAL SURGERY

A METHOD OF COMPARING ANALGESIC DRUGS*

BY

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Pain is a complex experience, and the comparison of pain-relieving drugs is complex also. Clinical trials of analgesics based on subjective reports are notoriously unreliable unless hedged around with stringent precautions to keep the patient and administrator in ignorance of what is being given. Similarly, estimations of pain-relief based on objective degrees of tranquillity tell us very little, for a patient can be made completely tranquil with drugs which make no pretence of analgesic action. Moreover, procedures such as these are qualitative rather than quantitative.

Hardy, Wolff, and Goodell (1940, 1952) have carried out quantitative comparisons of analgesics in experimental pain, using a machine called the "dolorimeter." This machine inflicts graded thermal burns, and has been the basis of a great deal of sound laboratory work, but for accurate results it must be used on trained subjects under standard conditions. Attempts have been made to equate the pain caused by this machine with naturally occurring pain (Javert and Hardy, 1951), but it is doubtful whether comparisons of such entirely different kinds of pain have any value (Haugen and Livingston, 1953). Ideally, analgesic drugs should be

*A paper read in the Section of Anaesthesia at the Joint Annual Meeting of the British Medical Association and the Canadian Medical Association, Toronto, 1955.

compared under the conditions for which they were designed—namely, in the presence of naturally occurring pain.

This paper is concerned with a method of comparison which is essentially related to everyday anaesthetic practice, and which is both objective and quantitative.

Pain in the upper abdomen restricts breathing to a marked degree. In 1927 Churchill and McNeil found that the vital capacity was reduced by 75% in the first twenty-four hours after gall-bladder operations, and by about 40–50% after lower laparotomies. In the same year Head found that pain could reduce the vital capacity to less than one-fifth of the normal value after upper abdominal operations. Modern anaesthesia has not changed this picture in any way.

Post-operative reduction of vital capacity is due to pain, to mechanical interference with the abdominal muscles, and, to a much smaller degree, to the pneumoperitoneum that is sometimes caused by trapping air during closure of the peritoneum in a relaxed patient. But pain is by far the greatest factor in reducing vital capacity (Cleland, 1949). Therefore an important aspect of post-operative analgesia is not only subjective relief of pain, although this is desirable, but also improvement of respiratory function, with the ability to cough and to breathe deeply.

Reduction of vital capacity by abdominal pain is shown most clearly when the pain is uncomplicated by the mechanical interference of operation—for instance, in acute pancreatitis or in acute perforation of a viscus. In these conditions restriction of respiration may be so severe as to cause cyanosis, but if the pain is relieved breathing is relieved also, and the cyanosis disappears. The case shown in Fig. 1 illustrates this point. The patient had already received papaveretum, ¼ gr. (22 mg.), one hour before the first vital-capacity tracing was taken, and he said, "I can breathe much better now since the injection," so one may presume that his vital capacity had been even lower before the opiate was given. Complete subjective relief by a sensory epidural block doubled his vital capacity, and repeated injections up the epidural catheter allowed painless deep breathing and coughing after operation.

Here, then, is an objective method for comparing the efficiency of analgesic agents in patients who have undergone upper abdominal operations. A drug which removes pain effectively will also restore the vital capacity closer to normal than one which does not relieve pain. Comparison of vital capacities after different analgesics will provide a quantitative indication of the amount of pain relief obtained with each drug (see Figs. 2 and 3).

If the vital capacity is measured before operation, and again after operation, when the patient is fully recovered from the anaesthetic and is in pain, we have a measure of the amount of respiratory impairment caused by the pain. Pain impairment becomes less after an analgesic drug is given, and the vital capacity increases in proportion to the

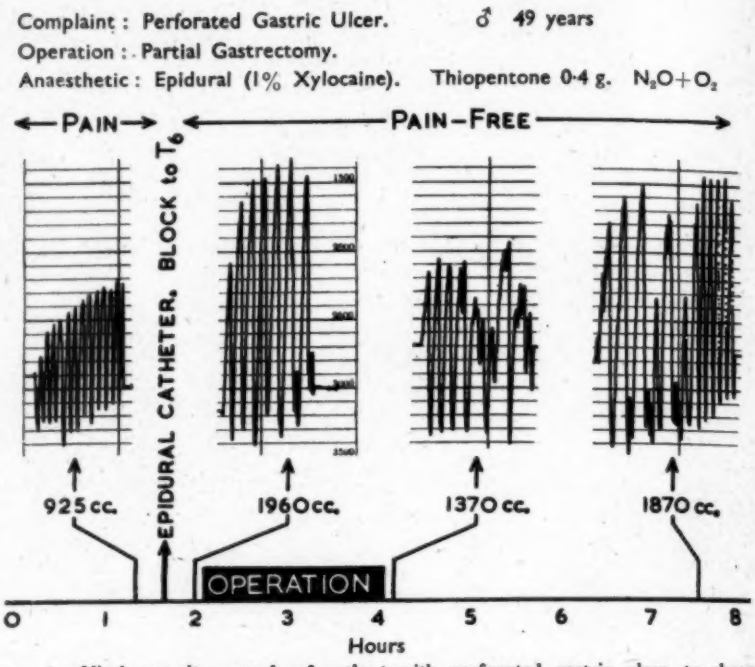

FIG. 1.—Vital capacity records of patient with perforated gastric ulcer, to show effects of pain and regional analgesia.

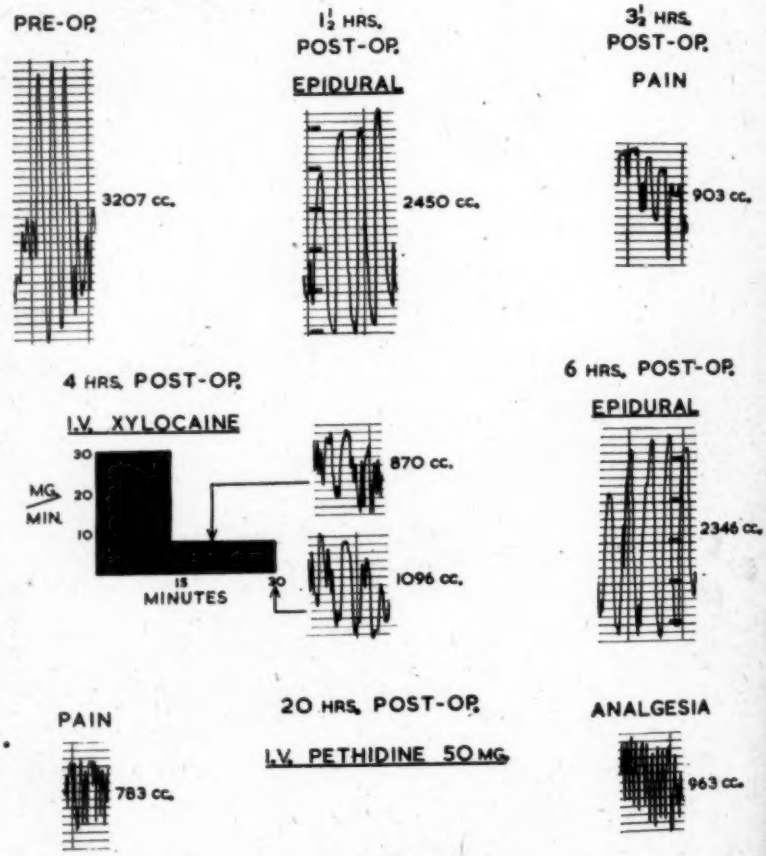

FIG. 2.—Vital capacity tracings from patient aged 30, before and after total gastrectomy (Case 3).

effectiveness of the drug. A perfect analgesic will restore the vital capacity to normal, or nearly normal, whereas an ineffectual drug will make no difference. If the amount of restoration of vital capacity is expressed as a percentage of the impairment caused by pain we arrive at a quantitative basis for comparing different drugs in the same, and also in different, patients. This percentage restoration of vital capacity (V.C.) may be called the respiratory restoration factor (R.R.F.) of the drug, and is a measure of its analgesic effectiveness (see Fig. 4). The R.R.F. is calculated thus :

$$\text{R.R.F.} = \frac{\text{Analgesic V.C.} - \text{Pain V.C.}}{\text{Pre-operative V.C.} - \text{Pain V.C.}} \times 100$$

The R.R.F. for any one drug will inevitably vary from patient to patient within a fairly wide range, but by carrying out serial readings in a sufficiently large number of cases it is possible to calculate the mean and standard deviation for the R.R.F. of each drug, and thus arrive at a reasonably significant comparison.

I have attempted to illustrate this method by comparing the R.R.F.s of three different types of post-operative analgesia in a group of 20 patients, using : (1) regional analgesia obtained by epidural spinal block, with an indwelling epidural catheter ; (2) systemic analgesia with (*a*) pethidine, and (*b*) methadone ("amidone") ; (3) systemic analgesia, using a local analgesic drug (lignocaine hydrochloride ; "xylocaine") by the intravenous route.

Method

In order to obtain an R.R.F. parameter wide enough for reasonable accuracy it is necessary to choose patients who are likely to suffer a deep depression of vital capacity in the first 48 hours after operation ; in practice, this means confining the series to upper abdominal operations and, possibly, simple thoracotomies. The day before operation the patient is instructed how to use the spirometer, and his co-operation is enlisted by pointing out the similarity between vital-capacity tests and the deep-breathing exercises he has already received from the physiotherapist.

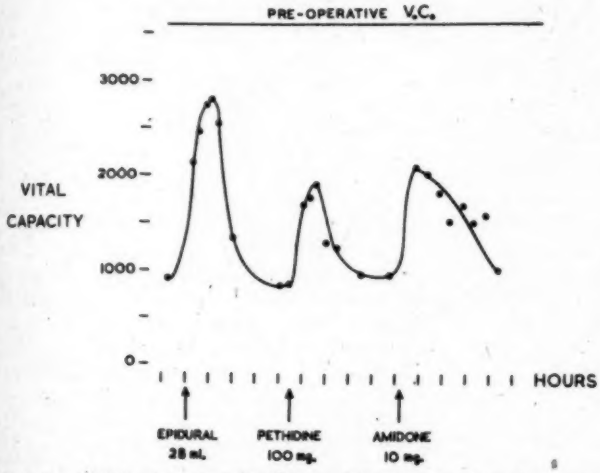

FIG. 3.—Serial vital capacity figures following total gastrectomy (Case 12).

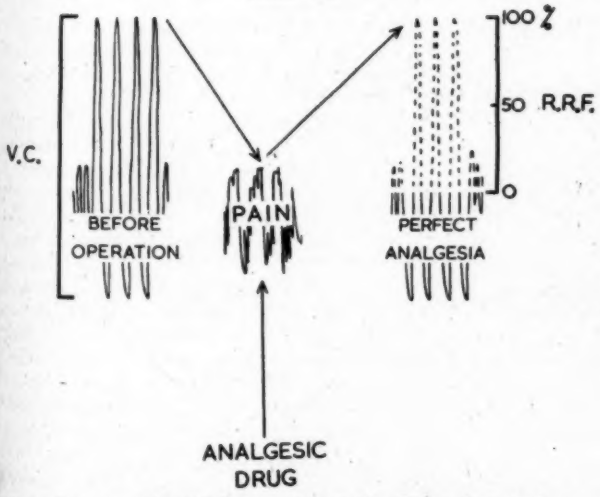

FIG. 4.—The respiratory restoration factor (see text).

Vital capacities are all taken in the supine position with one or two pillows, using a Benedict–Roth recording spirometer containing air, and a facepiece. The soda-lime tower is removed in order to reduce resistance to a minimum, and the spirometer is flushed out with air after each recording. A recording takes about one minute, and so one may ignore the respiratory stimulating effects of carbon dioxide accumulating in such short periods, because the CO_2 is diluted to negligible proportions by the large volume of air in the spirometer. With the facepiece firmly applied, the patient takes two normal breaths and then breathes in and out as deeply as possible four times in succession while receiving vigorous encouragement. The vital capacity is taken as the average of the three best expirations.

Premedication is light, or omitted altogether, and general anaesthesia is minimal, a sleep dose of thiopentone or hexobarbitone and nitrous oxide and oxygen being used. Relaxation is obtained with either an intravenous relaxant, in which case artificial respiration is carried out, or by means of a regional nerve block. When the effects of general and regional anaesthesia have worn off and the patient complains of pain, serial vital capacity recordings are started at intervals of 15–30 minutes, and two similar values obtained as a baseline for the "pain vital capacity."

The first analgesic procedure is then carried out, and serial spirometer recordings are taken until the vital capacity has risen to a zenith, and finally returned to its nadir as analgesia recedes. A second pain baseline is then obtained and the next procedure under test carried out. Two or more drugs or procedures may be tested in a series in this way.

For post-operative epidural analgesia a critically differential block is required, giving good relief of pain but the minimum of muscular paralysis. It was found that 0.8% xylocaine was best for this purpose. In order to keep the period of investigation within reasonable limits it was desirable that the epidural block should come to a peak and then wear off as quickly as possible, and therefore no long-acting drug such as cinchocaine was mixed with the xylocaine, and no adrenaline was added.

Pethidine was given in an approximate dosage of 1.4 mg. per kg. body weight, and amidone in one-tenth of this dosage. Both drugs were given intravenously.

Intravenous xylocaine was administered in the following way. A 0.5% solution was dripped in at a rate of about 2.5 ml. a minute until the patient became sleepy or confused. Signs of cerebral depression were taken to indicate saturation with the drug, and the drip was then slowed until a total of 400–500 mg. had been given in about 40–60 minutes. Serial vital-capacity readings were taken throughout this period, and following it for a further 30 minutes. In this way dosage was related to the observed central depressive effects of the drug, rather than to body weight, in order to be quite certain that a saturating dose had been given. Moreover, by continuing readings after the drip was stopped any evidence of analgesia without depression would be recorded.

Since the pain baseline may fluctuate slightly during the period of eight to sixteen hours when recordings are taken, the R.R.F. for each procedure is always calculated from the level of the "pain vital capacity" immediately preceding it. As a further precaution against errors arising from alterations in pain intensity, the order for the different analgesic procedures was varied from case to case.

Results

Curves for R.R.F.s calculated from serial vital capacities are shown in Fig. 5, and the figure for maximum vital

TABLE I.—*Vital Capacities and R.R.F.s in 20 Cases*

Case No.	Operation	Pre-Op. V.C.	Pain V.C.	Analgesia							
				Epidural		Pethidine		Amidone		I.V. Xylocaine	
				V.C.	R.R.F.	V.C.	R.R.F.	V.C.	R.R.F.	V.C.	R.R.F.
1	Partial gastrectomy ..	3,850	1,420	3,300	77·3	1,940	21·4				
2	,, ,, ..	2,560	1,110	1,970	59·3	1,095	−1·0				
3	Total ,, ..	3,205	905	2,470	68·0					1,096	8·2
4	Cholecystectomy ..	2,110	540 (before pethidine) 600 (,, amidone and xylocaine)	2,040	95·5	760	14·0	1,240	42·4	1,623	67·8
5	,, ..	1,300	860	1,470	138·5						
6	,, ..	2,660	1,425	2,850	115			1,595	13·8		
7	Partial gastrectomy ..	2,850	960	2,190	65·1			1,380	22·2		
8	,, ,, ..	3,660	1,700	3,380	85·5			2,400	35·6		
9	,, ,, ..	2,040	840	1,450	50·8	880	3·3	950	9·2		
10	Cholecystectomy ..	2,360	775 (before epidural) 900 (,, amidone) 850 (,, I.V. xylocaine)	1,960	73·5			1,030	11·9	1,090	15·9
11	Partial gastrectomy ..	2,630	1,070 (,, pethidine) 880 (,, amidone)			1,460	25·0	1,423	31·1		
12	Total ,, ..	3,580	950 (,, epidural and pethidine) 1,000 (,, amidone)	2,756	68·6	1,920	36·9	2,063	41·2		
13	Gastrostomy	3,060	1,660	3,453	136·5	2,070	29·3	3,080	101·4	2,186	37·5
14	Partial gastrectomy ..	3,000	1,000			963	−2·0	2,283	64·2	1,400	20·0
15	Cholecystectomy ..	2,446	1,000	1,896	62·0	1,070	4·8	1,433	30·0	1,300	20·8
16	Upper laparotomy ..	3,270	800	2,450	67·0	970	6·9	1,616	33·0	1,076	11·1
17	Partial gastrectomy ..	1,150	365 (before epidural and amidone) 450 (,, pethidine and I.V. xylocaine)	990	79·5	540	12·8	583	27·8	500	7·0
18	Cholecystectomy ..	2,500	1,100	2,703	114·5						
19	Partial gastrectomy ..	1,890	650 (before epidural and amidone) 510 (,, pethidine and I.V. xylocaine)	1,560	73·5	650	10·2	1,066	33·6	750	17·4
20	Upper laparotomy colostomy	770	380	816	111·8						

Each vital-capacity measurement is the average of the three largest in a series of four or five readings.

capacities and R.R.F.s in each case is shown in Table I, with the means and standard deviation in Table II.

It will be observed that in five cases the post-operative vital capacity under epidural block exceeded the pre-operative vital capacity by a significant amount. Four of these patients had signs of some degree of left-sided cardiac strain and pulmonary congestion. In patients with pulmonary congestion ventilation is improved and the vital capacity may increase by 20 to 30% following a moderate fall of systemic blood pressure caused by ganglionic or spinal blockade (Bromage, 1954, 1955), and this is probably the cause of the raised R.R.F. in these cases. Restoration of respiration beyond 100% clearly does not indicate a more than perfect analgesia, but merely an increased intrathoracic air space, and so these R.R.F.s have been reduced to 100% in calculating the mean epidural R.R.F.

R.R.F.s below the baseline in Fig. 5 occurred during periods of depression, when the drugs had made the patients too sleepy to co-operate fully in vital-capacity tests.

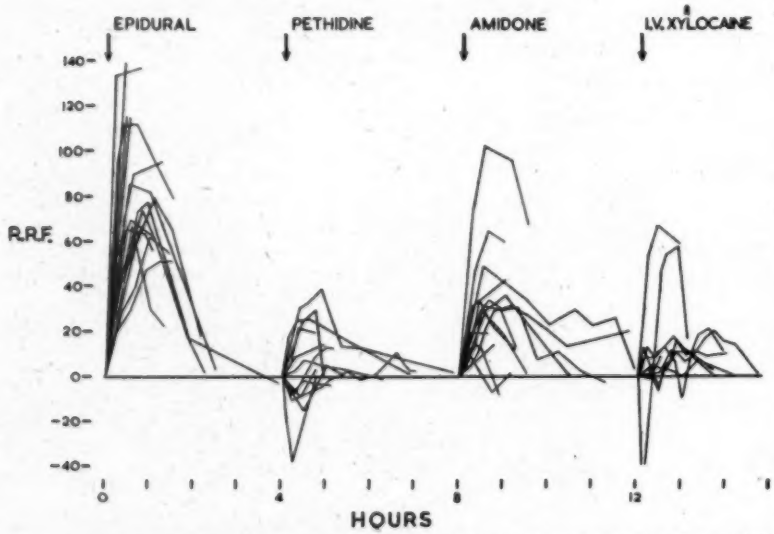

FIG. 5.—Serial R.R.F.s calculated from serial vital capacity tracings in 20 patients after upper abdominal operations.

TABLE II.—*Comparison of Maximum Respiratory Restoration Factors*

Procedure	No. of Observations	Mean R.R.F.	S.D. of Mean R.R.F. (corrected $\sqrt{\frac{n}{n-1}}$)
Epidural	17	80·2	16·4
Pethidine	12	13·5	12·3
Amidone	14	35·4	24·2
I.V. xylocaine	9	22·8	19·1

Discussion

The central problem of pain relief is to obtain analgesia without the depression which may unfortunately accompany it. If the object is merely relief of pain, regardless of other considerations such as depression, then there is no problem. But if we think in terms of function we must strive for purity of analgesia, with the minimum of functional depression. This investigation is directed to showing the resultant of these two opposing forces—the positive and negative aspects of pain relief.

As might be expected, regional nerve block, as illustrated by epidural blockade in this series, is paramount in the quality of analgesia produced. Restoration of respiration is not perfect for a number of reasons. The block must be very high to include afferent impulses from the diaphragm, and Cases 3 and 12 complained bitterly of shoulder-tip pain at the end of inspiration when all other pain was abolished. Also, for 100% restoration of vital capacity the block must differentiate perfectly between motor and sensory nerve fibres, for any degree of motor block will diminish intercostal activity in the analgesic segments, and, since patients differ in their sensitivity to analgesic drugs, it is unlikely that a perfectly differential block can be performed every time. The optimum concentration of xylocaine seems to lie between 0.7 and 1%, with 0.8% as the mean, and this latter concentration was used in most cases.

In the same way that a depressant concentration of regional analgesic produces a low R.R.F., so also systemic analgesics with a central depressant overlay result in a poor ventilatory performance. Pethidine and intravenous xylocaine have this disadvantage, which is shown clearly when contrasted with the relative purity of action of amidone. Local analgesics administered systemically can be effective if the speed of infusion is carefully regulated (Gordon, 1943; McLachlin, 1945), but the margin between effective analgesia and depression is narrow, and a drip rate that suddenly accelerates can rapidly lead to profound depression and dangerous convulsions. This lability in the balance between depression and analgesia is shown by the jagged peaks and valleys of the xylocaine series in Fig. 5. It would seem illogical to use local analgesics by the systemic route, unless the superior quality of analgesia provided were such as to warrant the close supervision required. This series shows no evidence of such superiority.

Clearly, the spirometric method of comparison would have to be modified if used for analgesic drugs having a direct respiratory stimulating effect of their own, for otherwise an abnormally high R.R.F. would be obtained, unrelated to the analgesia produced (something akin to the improvement of respiration found in the epidural series). This source of error could be eliminated by carrying out control vital capacities with a test dose of the drug before operation. The improvement of vital capacity that occurred following epidural block in patients with pulmonary congestion suggests that greater accuracy would be obtained by employing only patients with normal cardio-respiratory function in this type of investigation.

Lastly, it must be emphasized that the results of this method of comparison, based upon wound pain, may not be applicable to other types of pain. The method is deliberately designed to measure relief of pain in an inherently painful situation, whereas many analgesics act by removing the painful situation and not by dulling the pain. For example, a correctly applied Thomas's splint relieves the pain of a fractured femoral shaft, and the methonium drugs (although innocent of any essential analgesic action) may yet be most effective in the pain of acute pancreatitis (Davies *et al.*, 1953; Pyke, 1953). Similarly, although pethidine scores poorly in this series, it may be very valuable in pain from smooth-muscle spasm, such as ureteric colic, for then relief of pain is partly due to a direct antispasmodic action.

Summary

There is a need for comparing analgesic drugs quantitatively under clinical conditions. A quantitative method is described, based on vital capacity measurements. After an upper abdominal operation breathing is restricted by pain; analgesic drugs are assessed by the amount they restore the vital capacity towards normal.

The method is illustrated by comparing four analgesic procedures in 20 patients.

This investigation was carried out with the aid of equipment purchased by the Research Fund of the Association of Anaesthetists of Great Britain and Ireland.

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UVEOPAROTID SARCOIDOSIS WITH CEREBRAL INVOLVEMENT

A CASE REPORT

BY

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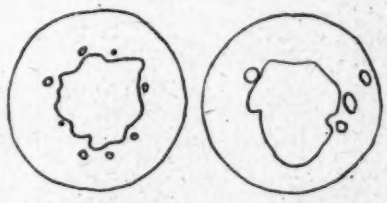
Heerfordt (1909) first indicated that the nervous system might be affected in sarcoidosis, and since then the occurrence of neurological complications has been widely affirmed. The attack is recognized to be usually upon cranial or peripheral nerves, and sarcoid of the brain or spinal cord is a distinct rarity. The following case of a man personally observed at intervals for over twenty years, and only recently dead, is therefore of interest, for he had a cerebral lesion at one stage of his illness. This presented as a slowly growing intracranial tumour which was surgically removed some 13 years ago.

Case Report

The patient, a van driver, was first seen when aged 24 as an out-patient in the ophthalmic department of the Cumberland Infirmary, Carlisle, on November 3, 1934. He complained that the sight in his right eye had begun to fail early in June that year, and the left eye six weeks later. In August he had developed bilateral parotid swellings, first on the right and three weeks later on the left, which had persisted since, and in October he had noticed a transient swelling on the left shin. On questioning it appeared that he had had an attack of left-sided chest pain, with shortness of breath, for some weeks in April and May, 1934, and a similar episode in 1931. There were no other significant points in the previous medical or family history.

On examination both eyes showed ciliary injection, fine keratic precipitates, a number of small pale nodules in the iris (eight in the right, four in the left: Fig. 1), and many posterior synechiae. The fundus was obscured by vitreous opacities. His visual acuity was less than 6/60. Both parotid glands and the right submaxillary gland were enlarged and hard. No other abnormal physical signs were found.



R.E. L.E.

FIG. 1.—Showing relative size and position of iris nodules.

The patient was admitted to the ward under the care of Dr. T. McL. Galloway, the results of whose special investigations were as follows:—chest *x*-ray examination: hilar glands enlarged bilaterally, lung fields clear; tuberculin tests: negative at 1/10,000, 1/1,000, and 1/100; blood W.R. negative; full blood count: red cells, 6,150,000; Hb, 125%; white cells, 4,700, normal differential count; urine: no albumin or sugar, no casts or cells, no tubercle bacilli; B.P., 138/80; no cough, no pyrexia. When discharged from hospital on January 30, 1935, the parotid swellings had subsided, the ciliary injection and the iritic nodules had gone, though some keratic precipitates and many vitreous opacities remained. Radiologically the hilar masses were still present, but were thought to have decreased somewhat in size. The diagnosis was chronic uveoparotitis.

The patient was seen at intervals during 1935 and once in 1936. The ocular signs regressed further, but he continued to complain of shortness of breath on exertion and easy tiring. Early in 1940 he had severe headaches; these increased in severity, and in consequence he had to stop

work in May of that year. On July 11, 1941, he again attended the ophthalmic department of the Cumberland Infirmary, now complaining of headache, fits, loss of memory, and failing vision. The fits were apparently

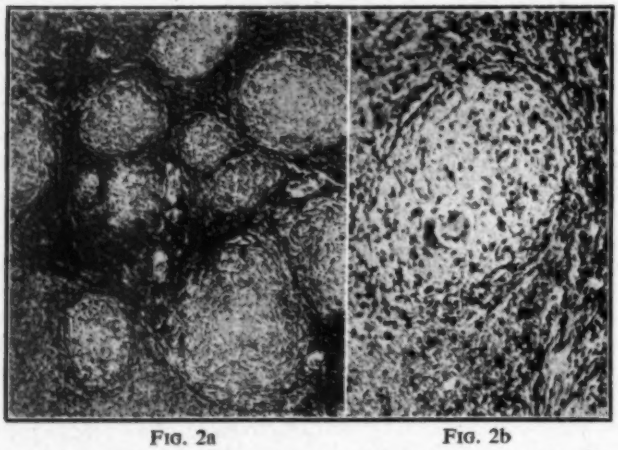


FIG. 2a FIG. 2b

FIG. 2a.—Operation specimen. Sarcoidosis in brain with epithelioid tubercles, calcification and giant-cell formation, but no necrosis. (×40.) FIG. 2b.—Same as Fig. 2a (×180), showing centrally placed giant cell inside epithelioid tubercle.

generalized and had started in November, 1940. On examination bilateral chronic papilloedema, with some secondary atrophy, was discovered. His visual acuity was 6/18 right and left. The visual fields showed right homonymous upper quadrantic loss. The pupils were irregular owing to posterior synechiae; there was patchy loss of iris pigment. The eyes were quiet and free from vitreous opacities. A diagnosis of cerebral tumour was made, and the patient was referred to Professor Geoffrey Jefferson on August 1, 1941.

FIG. 3.—Radiograph of chest done on August 17, 1950, showing hilar enlargement and egg-shell calcification of the gland.

On October 4 he was admitted to the Manchester Royal Infirmary under Professor Jefferson, who has kindly allowed me access to his case records. In addition to the signs previously noted, there was now a slight right-sided pyramidal disorder of movement in the arm and leg, and the patient's apparent loss of memory was found to be really due to nominal dysphasia. Skull *x*-ray films showed erosion of the posterior clinoids and dorsum sellae, no increase of vascular markings, and no intracranial calcification. A preoperative diagnosis was made of left temporal tumour—probably slowly growing glioma—and on October 14 an osteoplastic skull flap was turned. The temporal lobe was seen to be whitish, its gyri were widened and flattened. An avascular tumour was exposed in its substance, which had the macroscopic appearance of an astrocytoma. The tumour was excised by temporal lobectomy and sent for histological examination. The late Dr. Eugen Pollak, of the department of neuropathology, Manchester University, reported that it was not a neoplasm, but a conglomerate tuberculoma, showing "small heaps of epithelioid cells surrounded by lymphocytes and in some places single giant cells; miliary eruptions in different places with formation of more or less well-defined tubercles. In places there are the beginnings of cellular condensations, often of epithelioid character, in relation to vessel walls, and inflammatory lymphocytic infiltrations around vessels are also scattered through the specimen" (Figs. 2a and 2b).

In view of this report, it was feared that tuberculous meningitis might develop post-operatively, but convalescence passed uneventfully. A further chest *x*-ray examination showed the hilar shadows still prominent and what was thought to be a little fluid at the mediastinal end of the right interlobar fissures, but no evidence of disease in the lung parenchyma. The Mantoux test was also repeated, and found negative.

The patient returned home on November 2; neurologically, he now had a complete right homonymous hemianopia as the result of the temporal lobectomy, and right-sided weakness and dysphasia as before. His case was thought to exemplify the thesis that uveoparotitis was a form of tuberculosis, and for the next five years (until October, 1946) he was kept under review by Dr. J. A. Guy, Westmorland County Medical Officer of Health.

In 1950 I showed the slides from the cerebral lesion to Dr. J. Steven Faulds, pathologist to the Cumberland Infirmary, Carlisle. He commented that whilst the sections looked, superficially, like a tuberculous lesion in brain tissue, the histological characters were unquestionably those of a typical sarcoid granuloma. The appearance was of a mass of tuberculoid follicles, composed of endothelial cell systems with central hyaline necrosis, and containing giant cells of tuberculous type. The chief points of differentiation from tubercle were, firstly, the absence of caseation in the follicles, the centres of which still retained visible cell outlines, and, secondly, the central, rather than peripheral, situation of the giant cells.

In view of this new light on the patient's case he was readmitted to the Cumberland Infirmary in August, 1950. On examination abnormal physical signs were restricted to the eyes and nervous system. His visual acuity was 6/9 right, 6/6 left. Complete right homonymous hemianopia was present with sparing of the maculae. There was consecutive bilateral optic atrophy. Each eye showed atrophy of the iris stroma and thinning of the posterior pigment layer with radial dehiscences, but no scars at the site of the nodules seen in 1934. The pupils were irregular, with posterior synechiae; the vitreous was clear. Dr. Geoffrey Scott Harden reported:—Chest radiograph: areas of calcification and pleural thickening at apex of right lung; massive enlargement of hilar gland shadows bilaterally, with egg-shell calcification (Fig. 3). This type of calcification supports the diagnosis of sarcoidosis; it is not found in tuberculosis. *X*-ray films of the hands showed no evidence of bony sarcoid deposits. Blood count: Hb, 102%; white cells, 7,300 (polymorphs 59%, lymphocytes 24%, monocytes 3%, eosinophils 14%). Mantoux test: 1/1,000 weakly positive, 1/100 positive. The patient was well in himself.

Shortly after his return home it was noticed that he tired more quickly and movements and speech were more laboured. Towards the end of 1952 his interest in things and his power of concentration began to wane and he fell asleep during the day. In March, 1953, following a fit, his right arm and leg were considerably affected; so he was taken into Westmorland County Hospital, Kendal, under the care of Dr. G. M. Barrett, the consulting physician, to whom I am indebted for information about investigations carried out. These included a blood count which disclosed that the marked eosinophilia present in August, 1950, had completely disappeared, that the plasma proteins, including the albumin/globulin ratio, were normal, and that a liver biopsy revealed no change suggestive of sarcoidosis.

During that summer he had improved so much that he was able to take a daily walk of 500 yards. In January, 1954, after a similar attack, he was unable to clothe himself, to get about, or to take part in conversation, but remained cheerful and enjoyed company. On November 11, 1954, he had another fit, and on the 15th died in coma.

Dr. I. G. McGregor, who attended him, was able to arrange for a necropsy. This was done by Dr. Geoffrey W. Storey, assistant pathologist, Group Hospital Laboratory, Kendal, to whom I am indebted for a copy of his findings. Summarized these were:

Cause of Death.—Bilateral haemorrhagic necrosis of adrenals.

Adrenals.—No evidence of sarcoidosis present.

Brain.—Surrounding the site of the left temporal lobectomy there was softening, with a large number of pinkish miliary bodies. A similar area of infiltration in the right occipital cortex. Both areas confirmed histologically as active sarcoidosis (Fig. 4).

Thorax.—Enlargement of hilar and mediastinal lymph nodes—firm and rubbery, with patchy calcification and dense white areas, suggesting old tuberculosis. No evidence of old or recent tuberculosis in lung parenchyma. Histological examination confirmed that all glands showed active or old-standing sarcoidosis with calcification but no necrosis (Fig. 5).

Liver.—A few small foci of softening microscopically; these were found to be active sarcoidosis, but scanty in amount.

Discussion

This case was originally diagnosed in 1934 as one of uveoparotitis, a condition which at that time was generally believed to have a tuberculous cause (Souter, 1929; Garland and Thomson, 1933). The identity of the disease as a common presenting form of generalized sarcoidosis, later established by Waldenström (1937), Bruins-Slot *et al.* (1938), and others, was of course still unknown, but in retrospect it is now clear that the patient already had generalized lesions when he was first seen. In addition to the characteristic ocular and salivary gland involvement, he had had an attack of pleurodynia three years earlier which may have been significant; he had more definitely related pulmonary symptoms of chest pain and breathlessness some weeks before his eyes were affected, with enlarged hilar glands radiologically demonstrated later; and, further, the transitory painless lump on one shin, which was not seen, may well have been a dermal sarcoid.

In regard to the later development of cerebral symptoms, it appears that a neurological semeiology is far more often met with in the uveoparotid variant of generalized sarcoidosis than in the Boeck–Schaumann form of the malady (Jefferson, 1952), though the significance of this fact is obscure. Whether it is due to subtle variations in the agent which provokes the disease or whether it reflects differential tissue susceptibility of individual hosts is unlikely to be solved until the prime cause of sarcoidosis is discovered. At present there are three main hypotheses about the nature of the malady (Cowdell, 1954). The first, whose popularity is now distinctly on the wane, accounts it an atypical (anergic) form of tuberculosis infection. The second, which is of fairly recent origin, regards it as a diffuse tissue reaction of fixed pattern, which may be set in motion by any of a number of factors, and so considers it a syndrome rather than a disease proper. The third holds that it is unquestionably a true morbid entity, having a single cause as yet unidentified, but which may prove to be viral (Löfgren and Lundbäck, 1950). The present case provides no clues which bear on aetiology.

Mention has already been made of the infrequency of central nervous as compared with peripheral affection in sarcoidosis. From the reviews of Roos (1940) and Colover (1948), it is evident that only a relatively small number of such cases have found their way into the literature, and in most of them pathological proof has been lacking. Exceptions are the case described by Lenartowicz and Rothfeld (1930), in which there was very extensive sarcoid infiltration of the base of the brain, including the left temporal lobe,

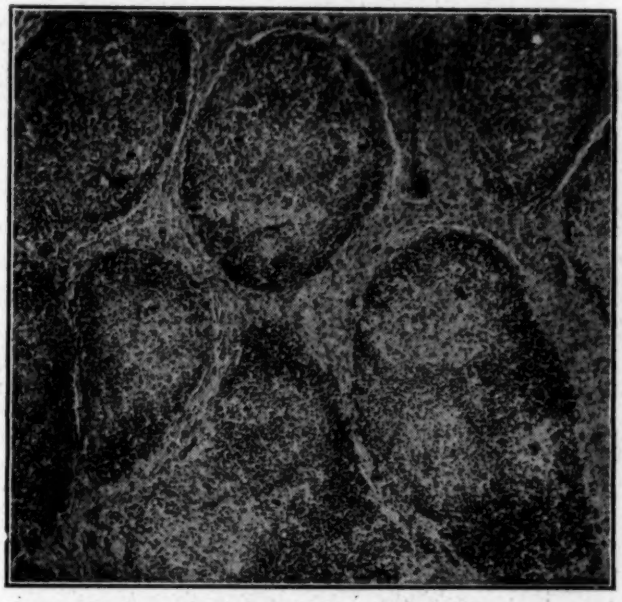


FIG. 4.—Necropsy specimen of left temporal lobe area, showing active sarcoidosis, with calcification. (×50.)

a case with brain and brain-stem lesions described by Zollinger (1941), and a case with hypothalamic involvement (Aszkanazy 1952); Tillgren (1935) and Wahlgren (1937) reported an intracranial sarcoid lesion restricted to the pituitary gland, and Naumann (1938) and Colover (1948) reported sarcoidosis of the intracranial meninges; but no

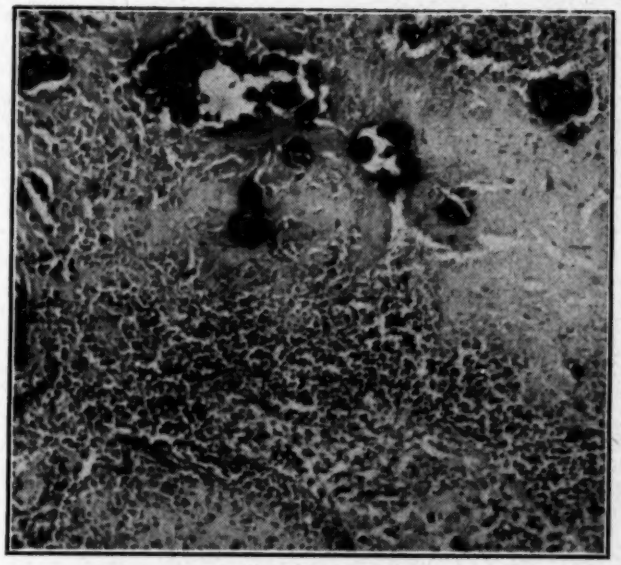


FIG. 5.—Hilar lymph node showing extensive fibrosis and calcification. (×80.)

others are known to me. The histology of sarcoid deposits in the neural substance is identical with the general pattern of sarcoid follicles in other tissues, and the microscopical appearance of the cerebral hemisphere lesion in the present instance conforms fully to this plan.

Lastly, it is remarkable how long a course the illness ran in this patient, for he lived 24 years after his first attack of

pleuritic pain in 1931 and over 20 years after the first proved evidence of sarcoidosis. One case is known to have survived over 40 years, but very few over 20 (Cowdell, 1954).

Summary

The case of a man with generalized sarcoidosis, personally observed for 20 years, is described. First seen in 1934 on account of uveoparotid symptoms, which afterwards subsided gradually, he presented himself again in 1941, now with signs of cerebral tumour. Diagnosis of a slow-growing glioma was made by Professor Geoffrey Jefferson, who excised the left temporal lobe. After histological examination, the tumour was pronounced to be an intracerebral tuberculoma, but re-examination of the histological sections nine years later by Dr. J. S. Faulds led to recognition that the microscopical appearances were, in fact, typically sarcoid in character. The necropsy revealed that the sarcoid changes were limited to the brain, the thoracic lymph nodes, and the liver. The eyes could not be reported on. Proved cerebral sarcoidosis is a very rare condition, and a brief review of the literature is given.

I gladly acknowledge my indebtedness to various colleagues, in particular to Sir Geoffrey Jefferson, to Dr. J. S. Faulds, and to Dr. J. M. Jefferson (University of Birmingham) for their interest and valued help. The photomicrographs were taken by Dr. Faulds.

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HYPERTONIC DEHYDRATION

BY

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The principles upon which fluid and electrolyte therapy are based are sound but often empiric. This empiricism applies particularly to the assessment of depletion when the patient is first seen and when data are minimal for subsequent treatment. The most reliable measures at this stage depend on our knowledge of the extracellular concentration of sodium and on our estimate of the total body water. When both these variables are known the total amount of each extracellular electrolyte can be calculated and the deficiency estimated.

In clinical practice Marriott (1947) has gone far to clarify our knowledge by insisting on the separate identity of "pure water" and "pure sodium" deficiency, though briefly mentioning a mixed type of deficiency. This mixed deficiency has been called by Darrow and Pratt (1950) hypertonic dehydration, and it is with this hypertonic dehydration that we are here concerned. It would appear from the observations of physicians examining the problems of water and electrolyte deficiency that hypertonic dehydration is not common (Marriott, 1947; Black, 1953). In surgical practice, however, it seems that hypertonic dehydration is common, not readily recognized, and but rarely treated.

Hypertonic Dehydration

It need scarcely occasion surprise that, in fact, water and electrolyte are rarely lost in proportion to their concentration in the extracellular fluid. Table I shows the simple

TABLE I.—*Electrolyte Content of Some Body Fluids*

Secretion or Effusion	Na (mEq/l.)	K (mEq/l.)	Cl (mEq/l.)
Stomach	60	12	130
Ileum	135	7·5	94
Peritoneal effusion ..	138	5	105
Sweat	50	15	50
Serum	140	5	103

arithmetic mean of the electrolyte content of various body fluids obtained in some of my own patients. The figures for invisible perspiration are taken as the upper limits of normal suggested by Darrow and Pratt (1950). The loss of pure water via the lungs and of hypotonic sweat, in conjunction with the loss particularly of gastric contents by vomiting, leads rapidly to a state of water and electrolyte depletion in which the water depletion is much more extensive than the electrolyte loss. This is only partly correct, in that the potassium loss by some of these routes represents a considerably larger fraction of the body store than would be lost if the potassium content were only that of the extracellular fluid. It is not intended, however, to treat at length with potassium deficiency, and attention is confined here mainly to the chief extracellular ions.

This loss of water in excess of electrolyte leads to a *rise* in the *concentration* of sodium and chloride in the extracellular fluid, although in fact the body store of these electrolytes has been depleted. In the case of a substance such as urea, which is diffused through all the body water compartments, this is not of importance, but in the case of the chief extracellular electrolytes, such as sodium and chloride, the extent of the space may be more important than the concentration of the ion. Haemoconcentration leads also to a rise in the haemoglobin and plasma protein content, often masking a concomitant deficit of these colloids.

As in a pure water deficiency, the excessive loss of water leads to a hypertonicity of the extracellular fluid, thereby resulting in a withdrawal of cellular water, though the extent of the changes is not so marked as in pure water deficiency. In the early stages this hypertonicity can also be offset by an increasing excretion of electrolyte in a concentrated urine. When, however, maximal renal concentration has occurred and the renal plasma flow continues to decrease, the kidney is no longer able to correct the increasing extracellular hypertonicity, and renal compensation is lost. If the maximal renal concentrating power is diminished—and this is not uncommon in the elderly male with prostatic symptoms—the onset of the clinical state is hastened. Hypertonic dehydration is seen particularly, therefore, in the older age group of male subjects.

This apparently simple explanation of hypertonic dehydration is unfortunately at variance with experimental observations. In particular, the experiments of McCance (1936) on salt deprivation have shown that the water loss parallels the sodium loss, and only at a much later stage does the serum sodium concentration fall. It appears from these experiments that osmotic tonicity is a consideration of greater importance to the body economy than is the regulation of the total body water. The relatively inaccurate observations of clinical practice, if they contradict these findings, must be viewed with suspicion. The fact, however, that such contrary results are observed is the justification for reporting the condition here.

Clinical Features

It has been variously reported that the symptoms of this state combine those of both pure water and pure sodium deficiency. It has been my own experience, however, that

the presenting symptoms are almost entirely those of a pure water deficiency. Patients with hypertonic dehydration present with marked thirst, an adequate peripheral circulation, a fairly full pulse, and a blood pressure just a little lower than would be expected for their age. The urine output is scanty, and the urine is highly concentrated and of high specific gravity, provided the kidneys are healthy. The most notable feature is that the concentration of sodium and chloride in the serum is near normal or above normal. In spite of the fact that these patients appear reasonably well, they are in a dangerous state, precariously balanced on the edge of peripheral circulatory insufficiency, and are quite unfit to undergo major surgical procedures. Table II shows the results of serial blood examinations in the following case.

Case 1.—A man aged 56 was admitted to a medical ward on November 2, 1952, suffering from organic pyloric stenosis. He was treated by gastric wash-out, but not with parenteral fluid or electrolyte therapy. Even on November 4 there was evidence of hypertonic dehydration, but this had become considerably

TABLE II.—*Hypertonic Dehydration* (*Case* 1)

Plasma or Serum Concentration	Nov. 4	Nov. 10	Nov. 15	Nov. 18
Cl_2 (mEq/l.) ..	102·5	114	92	90·6
Na ,, ..	132	148·5	123·5	127
K ,,	—	—	4·3	4·6
Urea (mg./100 ml.)	—	87	50	26
Hb	51%	70%	—	48%
Plasma proteins (g./100 ml.) ..	4·8	5·7	4·6	4·4

more marked by November 10. By this time the patient looked dehydrated, was very thirsty, but there was no evidence of peripheral circulatory insufficiency. He was transferred to a surgical ward on the 10th, and the evidence of hypertonic dehydration noted—namely, thirst, a rising serum sodium and chloride, a moderate increase in blood urea, and a rise in haemoglobin and plasma protein concentration. To uncover the true electrolyte insufficiency, sodium and chloride were replaced only in proportion to their loss by gastric suction and in the urine. In addition a 5% glucose infusion of 4 litres was given during the next few days and the blood again examined. It will be observed that the concentration of the extracellular electrolytes (except potassium) fell to subnormal levels although no new deficit of sodium or chloride had occurred. The urea and plasma protein concentration were also reduced as a result of the dilution effect. A further 2 litres of 5% glucose was then supplied, and the results on November 18 are shown.

It will be seen, therefore, that hypertonic dehydration presents clinically as one of a pure water deficiency, and that an examination of the extracellular electrolytes would suggest to the unwary that nothing is amiss. The electrolyte deficiency can be unmasked by giving a liberal supply of water by mouth if possible, and, if not, parenterally. In the case just described, the calculated sodium deficiency after hydration amounted to the equivalent of 4 litres of saline, a deficiency which would have remained unsuspected if adequate hydration had not been attempted.

Dangers of Untreated Hypertonic Dehydration

The dangers encountered when hypertonic dehydration is neither suspected nor treated are seen mainly in surgical patients and only infrequently in the unoperated. Study of Table II will show that an anaemia and a hypoproteinaemia of considerable degree have been uncovered during the process of hydration. The example demonstrated did show evidence of anaemia before hydration, but frequently the anaemia is not uncovered until the hypertonicity is corrected. Under these circumstances the haemoconcentration remains unsuspected, and at operation is intensified by the present practice of using 5% dextrose as the vehicle for anaesthetic drugs. It has become almost axiomatic that, provided renal function is reasonable, no harm can result from the giving of excess water. What is not required will be excreted. In unsuspected hypertonic dehydration, however, the water will be retained, and a sudden post-operative fall in concentration of haemoglobin, plasma proteins, and electrolyte results. To the danger of an unsuspected anaemia, an unsuspected hypoproteinaemia is added.

Before operation it is only rarely possible to produce oedema, even in an example such as Case 1, by this dilution phenomenon unless saline is given. It will be observed from the protocol in that case that even on November 18 a marked hypoproteinaemia was produced. The next step in treatment is to correct this by supplying plasma or, as in this particular instance, to correct the hypoproteinaemia and anaemia by blood.

When the hypoproteinaemic state is not uncovered until the post-operative phase, however, oedema is very apt to occur simply by supplying water. As the adequate supplement of water is thought to be without danger in the post-operative phase the danger is not readily appreciated. In other cases water intoxication may occur, and it is possible that the rare cases of water intoxication encountered in the post-operative period are due to an unsuspected pre-existent hypertonic dehydration which has not been corrected before operation, and which has led to water retention in the post-operative phase. A water retention of slight degree is normal after even uncomplicated operation (Moore and Ball, 1952; MacPhee, 1953), but the water retention here discussed is much greater and must be regarded as a danger to the patient. Such an unfortunate result is all too common, and may be represented by the following example.

Case 2.—A man aged 60 was admitted to a surgical ward on September 7, 1952, with a gastric carcinoma. Gross dehydration was present, the blood analysis being shown in Table III. The progress on September 9 and 10 is demonstrated. The low serum protein concentration, however, went unmarked, and operation

TABLE III.—*Blood Analysis in Case* 2

Plasma or Serum Concentration	Sept. 8	Sept. 9	Sept. 10	Operation	Sept. 11	Sept. 12
Cl_2 (mEq/l.) ..	104	106	113		99	89
Total protein (g./100 ml.)..	5·2	—	—		—	—

was carried out on the 10th. The daily sodium and chloride loss was corrected each day in the post-operative phase, but in addition 1 litre of 5% dextrose was supplied daily in excess of requirements. By September 12 the patient had become grossly oedematous, and, although no sodium had been given in excess, a condition of water-overload had been established. Plasma was then ordered, but it was too late, and the patient died that day. Necropsy showed extensive tissue oedema, pulmonary congestion, and oedema.

The features in this case are complicated by an uncorrected metabolic alkalosis, but this would not have led to a fatal outcome. The fact that a degree of hypertonic dehydration remained unsuspected, and that the plasma protein concentration, though initially low, was never re-estimated, permitted a dangerous hypoproteinaemia to result in the post-operative phase.

Conclusions

It has been suggested, therefore, that the concentration of extracellular electrolytes may be no guide to the actual state of the body economy. Decrements in total body water may occur at a different rate, and to a different extent, from losses of sodium and chloride. When time is available before surgical treatment becomes necessary, adequate hydration of the thirsty patient should be undertaken and serial haematocrit readings should be obtained.

Many methods of assessing extracellular electrolyte deficiency in the depleted patient have been published, and most are reliable. They depend, however, on the assumption that changes in water volume and electrolyte concentration march together. Where doubt arises, however, it should always be possible to supply the patient with a loading

dose of water and then repeat the serum electrolyte examinations. If the water is not required in the pre-operative state it will rapidly be excreted, but if required it will be retained and the dilution effect described will take place.

Summary

If water is lost in excess of extracellular electrolyte a state of hypertonic dehydration may be induced.

In this condition the concentration of extracellular electrolytes may be normal or even above normal when the total quantity of electrolyte is decreased.

In the post-operative phase oedema may result if water is given in excess.

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EARLY IMMUNIZATION AGAINST WHOOPING-COUGH

BY

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Whooping-cough has rightly been described as one of the most prevalent and certainly the most lethal of acute specific infections of childhood (Parish, 1952): it caused 9,401 deaths in England and Wales in the ten years preceding 1951, 50% of which were in babies under 1 year old. American workers noted that approximately half their deaths from pertussis occurred in infants who had not yet reached the accepted age for immunization (Fox and Snartemo, 1949). It is also generally agreed that the younger the victim the greater is the severity of the disease and its attendant complications and sequelae.

Although the prophylactic uses of pertussis vaccine had previously been demonstrated (Madsen, 1925; Kendrick and Eldering, 1936; Sauer, 1933), immunization at an early age did not yield what appeared to be favourable results till 1947 (Sako, 1947). It was observed that infants under 3 months of age developed agglutinins as satisfactorily as those in any age group, and that 75% of infants under 6 months developed agglutinins.

Di Sant' Agnese (1949) recommended active immunization against pertussis as soon as possible after birth. In his series inoculations of combined pertussis, diphtheria, and tetanus antigen were completed at nine weeks after birth, and at 13 weeks 60% of these babies had pertussis agglutinin levels which were considered to be protective. It should be stated, however, that agglutinin titres are not accepted by all workers as an index of protective function.

Some investigators suggested that the variable response to early immunization might depend on the type of vaccine used; it was also thought that a more prolonged stimulus was required in young babies, and that this was provided by alum-precipitated vaccine (Sako, 1947). Disappointing results in young infants followed the use of fluid (suspended) vaccine (Sauer, 1941) and many more febrile reactions were observed with it. Howard (1950), in a progress report, noted the alum-precipitated vaccine to have fewer side-effects, but it has been stated that severe or serious reactions occur with it because it causes more local trauma than the other types (Cockburn, 1951).

In the M.R.C. trial (1951) good clinical results were obtained with all five types of vaccine used, but great variability was disclosed. Suggested reasons for this included: (*a*) the selection of strains; (*b*) the medium on which the organisms for vaccine were grown; (*c*) the methods of harvesting the growth; or (*d*) the nature of killing and preserving agents.

With the foregoing facts in mind, we proceeded to investigate the results of immunizing babies at an early age with two different sorts of vaccine, and, further, we felt it would be of interest to observe whether there was an appreciable antibody level in babies at birth, and whether the naturally occurring antibody bore any relationship to the one produced by immunization.

Methods and Materials

All sera were tested against six antigenic suspensions. One was kindly supplied by Glaxo Laboratories Ltd., and consisted of a formolized suspension of two strains of *H. pertussis* containing $2{,}000 \times 10^6$ organisms per ml. in saline. The remaining five suspensions, of approximately the same number of organisms, were prepared from strains grown according to the technique described by Lacey (1953, personal communication). These were *H. pertussis* H5 and *H. parapertussis* 15 grown in both X and C modes, and *H. pertussis* H16 in the X mode only.

A high-titre rabbit serum prepared against the Glaxo antigenic suspension was used as a positive control.

The material for immunization was obtained as a commercial vaccine in two forms—an aluminium phosphate adsorbed preparation and a simple suspension. These were labelled A and B respectively for the purpose of the investigation.

Titration Technique.—Tests were made in 0.5 by 5 c.cm. tubes. Doubling dilutions of serum were made in saline, starting at a titre of 1:8 and concluding at 1:512. An equal volume of antigen was added to each dilution, and the tubes after mixing were placed in a water-bath at 37° C. for two hours. The final readings were made after allowing the tubes to stand overnight at room temperature. Only definite agglutination was read as positive, faint granularity and similar reactions being disregarded. Figures were recorded as serum dilutions; that is, the final dilutions were in fact double these. Dry, clean tubes were used to collect cord blood at delivery and maternal venous blood shortly after. Blood from the babies at 6 months of age was obtained by heel pricks and collected in Wright's capsules. Sera were separated and stored at −20° C. until tested.

Selection of Cases.—Cases were selected by choosing at random mothers who came to the antenatal clinics between certain fixed dates; these had the nature of the experiment explained to them, and 90 volunteers were divided into three groups of 30 each. Their case records were labelled A, B, and C. Group A babies received aluminium-adsorbed vaccine, Group B had suspended vaccine, and Group C had no immunization before 6 months and served as a control group: they were offered immunization at 6 months.

The basic plan of the investigation consisted in determination of the antibody level against the strains of *H. pertussis* and *H. parapertussis* described above, in mothers and babies at delivery, and in the babies at 6 months. Unfortunately there were defections. Some mothers changed their minds and refused immunization after their babies had been delivered, and some babies were excluded because of illness or congenital defects. There were also a few cases with incomplete injection records.

Immunization.—Babies in both groups were given three injections. Group A babies received 0.5 ml. of the aluminium-adsorbed vaccine intramuscularly at 8 to 14 days of age, 6 weeks, and 3 months. Group B babies received 1 ml. of suspended vaccine at the same intervals. No severe or untoward reactions to the injections were reported.

Results

Of 78 maternal sera tested 18 contained an antibody, whereas of the 76 baby sera tested 36 contained an antibody. However, in just under half these babies the cord titre was 1:8 or a weak 1:16 only, so it seems that the corresponding maternal antibody may have been too weak for demonstration at 1:8.

Where there was a demonstrable maternal antibody there was always a corresponding antibody in the cord blood, with one exception, and in this case the maternal and cord antibodies were different and both of low titre. The titre in the cord blood was usually one or two tubes higher. The most frequently occurring antibody in both cord and maternal blood was the one against the parapertussis strain (XPA15) grown in the X mode by Lacey's method (Tables I and II).

TABLE I.—*Number of Cord and Maternal Sera which Contained Antibodies to One or More of the Antigenic Test Strains*

	Cord	Maternal
Total No. of sera tested	76	78
No. containing antibodies	36	18
To commercial antigen	2	3
„ parapertussis strain XPA15	28	12
„ „ „ CPA15 ..	—	—
„ pertussis XH16	—	—
„ „ XH5	—	—
„ „ CH5	1	—
* „ both commercial antigen and XPA15	4	3
„ pertussis XH16 and XPA15 ..	1	—

* The titre to XPA15 was higher in all but one case.

The antibody produced in response to immunization with the commercial vaccine was specific for it. The immunized babies who had developed titres to the commercial vaccine at 6 months had lost their natural antibody by that time, with the exception of two in whom an antibody to the commercial antigen was present at birth. One of these also showed an antibody to the XPA15 strain, and the titre of this had fallen considerably at 6 months. In all the remaining babies which had a passive immunity at birth, the antibody was not detectable at 6 months. One baby that had been immunized with vaccine A was reported by its mother to have had a mild attack of whooping-cough which was treated by her own doctor, and in this child the titre at 9 months had risen from 1:32 to 1:128 for the commercial antigen. The naturally occurring antibody at birth was a weak one against the XPA15 strain and was lost by this time.

All 15 babies immunized with the aluminium-adsorbed vaccine A developed a titre by 6 months, whereas only 3 of the 15 babies immunized with suspended vaccine B did so. Further, the vaccine A titres at 6 months were considerably higher than the vaccine B titres—the highest titre observed with the former being 1:256, and with the latter a weak 1:32. In the baby whose birth antibody was one for the commercial antigen alone, the titre rose after immunization from 1:8 to 1:64, and in the baby whose birth antibodies occurred to both the commercial antigen and XPA15, the former was enhanced by immunization, while the latter diminished till only just detectable at 1:8. Vaccine A was used in both these cases.

Of the 18 mothers in whom a demonstrable agglutinin was found at the time of delivery, three had an antibody level equal to that of the cord blood, three had a higher level, and 10 had a level only half as high as that of the cord. Of the remaining two, one had a different antibody from the corresponding cord blood, and from the other no cord blood was received.

Discussion

Although complete records were obtained for the full inquiry in only 50 cases of the original 90, satisfactory numbers are available to provide some interesting conclusions.

Only 18 of the 78 mothers tested had a demonstrable antibody against the test suspensions used, and it seems reasonable to suppose that had many more different suspensions been available for testing them more maternal sera might have shown the presence of an antibody.

In all but the one case in which the cord and maternal antibodies were different, the antibody found in the maternal serum was also present in the baby's serum. In addition, there were 18 babies who showed a just detectable antibody in the cord blood when the mother's serum gave no results. It was presumed that in these cases the maternal antibody was weaker in titre than the first dilution (1:8) used in the titrations. In 10 out of 18 instances the antibody titre in the cord blood was at least twice that of the corresponding maternal blood, and in only three cases was the maternal titre higher than that of the cord blood. These findings are in agreement with previous observations in regard to other antibody systems: Barr *et al.* (1949) in diphtheria, and Murray *et al.* (1950, 1953) in staphylococcal antihaemolysin and streptolysin.

All babies but one had lost their natural antibody (where this was not one against the commercial antigen) by the age of 6 months, and this would seem to suggest a reason for immunization before that age. It was noted by Mushulow *et al.* (1941), Lapin (1942), and Miller *et al.* (1943) that in young infants the height of the antibody titre was reached two to four months after completion of immunization, with a "plateau effect" lasting three years or more.

The presence of an antibody in the baby's blood at birth seemed to have no blanketing effect on immunization, titres being developed in immunized babies whether or not they already possessed an antibody. In the two cases in which the antibodies present corresponded to the commercial

TABLE II.—*Incidence of Naturally-Occurring Antibodies at Birth and at 6 Months, and Response to Immunization with Vaccine A and Vaccine B (50 Cases)*

	Vaccine A (15 Cases)			Vaccine B (15 Cases)			Control C (20 Cases)		
	Birth	6 Months		Birth	6 Months		Birth	6 Months	
		Natural Antibody Still Present	Antibody to Commercial Strain		Natural Antibody Still Present	Antibody to Commercial Strain		Natural Antibody Still Present	Antibody to Commercial Strain
Commercial strain	1	1 Same case	1	0	—	—	0	—	—
XPA15	6	0	6	6	0	1	9	0	—
Commercial strain and XPA15 ..	1	1* „	„ 1	2	0	0	1	0	—
Other strains as in Table I ..	0	—	0	0	—	0	0	—	—
Totals with antibody	8	2	8	8	0	1	10	0	—
No antibody at birth	7		7	7		2	10		
Total	15		15	15		3	20		—

* Titre to XPA15 considerably diminished.

strains being used for immunization, the titres rose from 1:8 to 1:64, and from 1:8 to 1:32. Howard (1950) noted that antibody titres were definitely associated with immunity as judged by clinical criteria; according to Miller and Ryan (1948) there was no susceptibility where there was a titre, though immunity could exist without there being a demonstrable titre; the attack rate varied inversely with the titre. Paschoud (1952), in mouse-protection experiments, observed that rabbit-immune sera with a high agglutinin titre were also highly effective in protective function, although McGovern (1950) stated that agglutinin value did not correlate closely with the degree of protection afforded (mouse tests). Mishulow *et al.* (1941) had observed that the titres of agglutinating antibodies did not parallel the occurrence of protective antibodies, and stated further that there was no evidence that the antibody titre was an index of resistance to the disease.

In the present investigation laboratory methods demonstrated a specific response to the commercial antigen only, there being no accompanying rise in the titres of the naturally occurring antibodies. Indeed, all but one of these had disappeared by the time the final tests were made at 6 months.

In view of the recognized existence of strain variation and related antigenic changes in *H. pertussis* (Bordet and Sleeswyk, 1910; Bordet, 1912; Standfast, 1951; Lacey, 1951), and of the role of *H. parapertussis* in causing much "so-called whooping-cough" (Halpern and Halpern, 1948; Miller and Ryan, 1948), the production of a universally efficient vaccine seems to be a question still open to discussion. It has been noted by Ungar (1954) that pertussis vaccines do not protect laboratory animals against *H. parapertussis* infections.

By the test-tube methods described above, the aluminium-adsorbed vaccine appeared to elicit a better response than the plain suspension.

Summary

A brief review of work on pertussis immunization in babies is given.

Details of an investigation into the possibilities of early immunization, and the laboratory techniques used, are described.

Antibody levels at birth were found in about half the babies tested. All babies but one had lost their natural antibody by the age of 6 months. More than one type of natural antibody occurred in the series.

Appreciable agglutinin titres were obtained in all babies who received the aluminium-adsorbed pertussis vaccine. A poorer response was achieved with the suspended vaccine.

The presence of a naturally occurring antibody in the cord blood did not affect the production of an antibody in response to immunization.

Response to immunization as indicated by laboratory methods was specific for the commercial antigen.

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EVALUATION OF THE RAT OVARIAN HYPERAEMIA TEST FOR PREGNANCY DIAGNOSIS

BY

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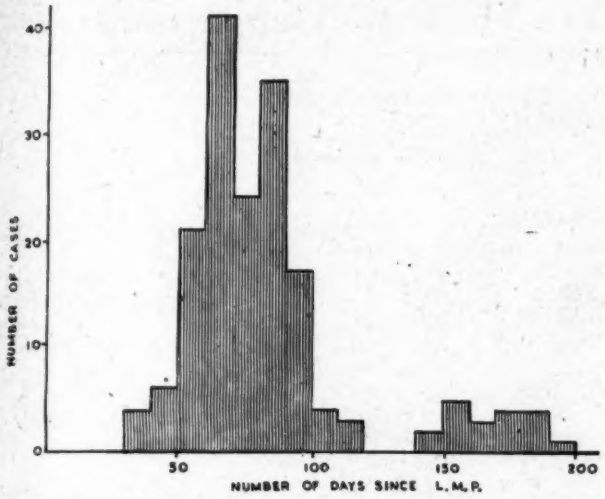
Immature rats are more resistant than mice to toxic urines (Evans and Simpson, 1930), and after treatment with gonadotrophin their ovaries show easily recognizable hyperaemia (Zondek, 1926). This reaction was first utilized by Reiprich (1933, 1934) for purposes of a pregnancy test. Since that time the method has aroused considerable interest and numerous workers have reported on it favourably (Walker and Walker, 1938; Kelso, 1940; Frank and Berman, 1941; Salmon *et al.*, 1942a, 1942b; Kupperman *et al.*, 1943; Soman, 1944; Kaminester, 1944; Ramsey *et al.*, 1944; Kupperman and Greenblatt, 1944; Kline, 1944; Aschheim and Varangot, 1945; Sala *et al.*, 1945; Hinglais and Hinglais, 1947; Riddell, 1949). Positive results may be obtained as early as two hours after subcutaneous injection or even one hour on intravenous injection (Sturgis and Haour, 1951). Most workers, however, used longer periods ranging from 6 hours to 18 or 24 hours, and the latter apparently led to more accurate results (Zondek *et al.*, 1945).

Rakoff and Fried (1947) found that the administration of a pituitary extract increased the sensitivity of test animals to urinary chorionic gonadotrophin and suggested this as an improvement of the test (Fried and Rakoff, 1949, 1950). The use of the pituitary synergist has, however, proved unsatisfactory in the hands of other workers (Hoffman *et al.*, 1951). Farris (1944, 1946, 1950) was the first to draw attention to false-positive results: he stated that during the normal menstrual cycle erroneous results may be obtained for three or four days. These findings were disputed by Kupperman and Greenblatt (1946) and Bunde (1947), who found that in their series all the errors were false negatives. However, since then an increasing number of workers have reported false-positive findings in their control material (Behnken *et al.*, 1948; Fried, 1948; Riley *et al.*, 1948; Dubrauszky, 1950; Kelsey *et al.*, 1950; Hoffman *et al.*, 1951). Furthermore, different authors used different techniques: the number of rats per test, the strain, the mode of inoculation (subcutaneous, intraperitoneal, intravenous) all varied as well as the total volume of urine injected. Readings were taken at 1, 2, 3, 6, 18, or 24 hours afterwards, and the criteria of accepting a positive result were also at variance. Many of the workers compared their results with the Aschheim-

Zondek or the Friedman test; others found their clinical material difficult to analyse, since false-positive findings could be ascribed to abortion.

In the present inquiry, instead of following-up retrospectively a proportion of the routine tests performed—the approach used by other investigators—known pregnant and non-pregnant healthy individuals were tested. It was felt that a clinical series analysed retrospectively may be misleading, since only a small proportion of cases can be followed up: owing to the moral and personal issues involved the answers obtained are likely to be biased. The positive material used consisted of



Histogram showing periods of gestation of positive controls at time of testing.

early morning specimens of urine obtained from women attending an antenatal department. The time since the last menstrual period varied from 30 to 200 days, with the majority around 50 to 100 (see Figure). The negative material was obtained from healthy female laboratory workers and nurses.

Technique

The tests were carried out by injecting 2 ml. of early morning urine, untreated in any way, subcutaneously into immature female rats 3 to 6 weeks old. The Wistar No. 1 strain was used, and this stock showed unchanged sensitivity to gonadotrophin through a period of several years. Titrations carried out from time to time always showed sensitivity ranging from 2 to 3 I.U. per rat, corresponding to 1,000 to 1,500 I.U. per litre of urine (Albert, 1949). Readings were taken 18 hours after injection. The animals were anaesthetized by chloroform and the abdomen was opened while the animal was alive. The ovaries were exposed and their colour was observed against the peritoneal surface of the abdominal wall and compared with the colour of the Fallopian tubes. The normal ovary of the immature rat has a dull, waxy, yellowish colour. The effect of gonadotrophin consists in varying degrees of hyperaemia and usually some swelling. This contrasts with the background of the abdominal surface, which has the colour of the normal ovary. Occasionally only one of the ovaries shows the positive change. The readings have to be taken immediately after opening the abdomen, and the animal is afterwards killed by exsanguination.

The simplicity of this test is its main advantage. The urine requires no treatment or concentration. In over 300 tests only 3 specimens killed the rats. The reading, however, requires practice and good light. Satisfactory readings cannot be taken by fluorescent light. Unless the ovaries are looked at within one minute of opening the abdomen, false-positive readings may result, as the ovaries turn pink on exposure to air. False-negative results may be obtained if the animal dies before the reading is taken, as hypostasis may drain away the hyperaemia. Likewise exsanguination blanches the ovaries within seconds, and must be avoided. Occasionally all the abdominal organs are found to be intensely red—in these cases satisfactory readings cannot be taken. Urine from patients treated with penicillin is also said to lead to false-positive results (Blaich and Gerlach, 1950).

Results

The findings obtained, using a single rat per specimen, are shown in Table I. With the "one-rat" test a false-negative finding was obtained in 1 out of 14.2 cases and a false-positive finding in 1 out of 13.7 cases. Part of this material was also examined by means of the Hogben test, through the kindness of Dr. H. Schwabacher, and a comparison is shown in Table II. The rat test gave a slightly greater number of correct positives, but while the toad test does not give false positives the "one-rat" test fails in this respect. The greater recovery of correct positives may be due to the nature of the material (see Chart) since many of the specimens were from advanced pregnancies with falling gonadotrophin output at a stage when a test would hardly be required for clinical purposes. The disagreement between the two tests was 18.1%. A positive rat test and negative *Xenopus* test were obtained in 12.8%, while the reverse was found in 5.3%. A false-negative result by both tests was obtained in only 0.5% of pregnancies. In these cases the output of gonadotrophin was probably deficient, but all the other discrepancies must be attributed to variations in the animals used. The false-positive results obtained with the rat test are not due to the injection of urine: such findings were also encountered occasionally with uninoculated control animals.

TABLE I.—*Results of* 282 *Rat Ovarian Hyperaemia Tests*

	Total Tested	Correct	Wrong
Known pregnant	227	211 (93%)	16 (7%)
Normal controls	55	51 (92·7%)	4 (7·3%)

TABLE II.—*Comparison of* 204 *Rat Ovarian Hyperaemia and Hogben Tests*

	Known Positives		Negative Controls	
	Correct	Wrong	Correct	Wrong
Rat test	162 (93·1%)	12 (6·9%)	27 (90%)	3 (10%)
Hogben test ..	150 (86·2%)	24 (13·8%)	30 (100%)	0 (Nil)

Discussion

Since the laboratory diagnosis of pregnancy is often invoked for cases requiring operative termination of gestation, even an occasional false-positive finding may be of serious importance and the percentage of positives recovered is not a true measure of the clinical usefulness of the test. It is clear that the rat ovarian hyperaemia test carried out on single animals is unsatisfactory for clinical use, since false negatives will be obtained in about 7% of the cases, and, what is more important still, false positives in about the same percentage. By increasing the number of animals used, the statistical odds of obtaining a correct answer can be greatly improved, however.

While the original Aschheim–Zondek test required six immature mice, the Friedman test was generally carried out on a single rabbit for reasons of economy. All later biological tests followed this trend of economy and suffered in accuracy as a result. This is well illustrated by the statistical analysis of the "one-rat" test, which shows that by increasing the number of animals any desired degree of accuracy can be achieved. The calculations were based on the assumption that all the errors were due to the test animals, and the rare cases where failure of gonadotrophin excretion occurred were left out of account. It must also be stressed that the

estimate of proportion of errors has a fairly large sampling error. The expectations depend on the expansion of the binomial $(p+q)^n$, where p is the probability of obtaining a false result. Table III shows the reliability of the test with

TABLE III

No. of Rats Used	Error if all Animals Give Same Result	Repeat rate (One or More Animals Giving Divergent Results)
2	1 in 173	1 in 7·6
3	1 „ 2,250	1 „ 5
4	1 „ 29,450	1 „ 4
5	1 „ 400,300	1 „ 3·3

increasing numbers of animals if all the animals give either positive or negative results. In a high proportion of cases the answer will not be clear-cut in the sense that one or more animals give divergent results. In these cases a repeat test would be required and the repeat rate has also been calculated.

For most purposes a "two-rat" test would combine a sufficient degree of accuracy with a relatively low repeat rate. If a rapid answer is needed four rats should be used (Table IV). If all agree the chances of error are negligible,

TABLE IV

No. of Rats Used	Result	Chances of Error	Repeat Rate (Two or More Animals Giving Divergent Results)
2	AB	1 in 1	0
3	AAB	1 „ 70	0
4	AAAB	1 „ 5,536	1 in 32
5	AAAAB	1 „ 42,750	1 „ 19

and if one disagrees the chances of error for the remaining three are still only 1 in 5,500. The 3 to 1 ratio will occur with tolerable frequency, and only very few tests will have to be repeated.

This approach allows a more critical test when clinical urgency or importance warrants the added expense.

Summary

The rat ovarian hyperaemia test was carried out on 282 samples of urine. When one rat per test was used a slightly greater number of correct positive findings were obtained than with the Hogben test, but the rat test gave a considerable number of false-positive results. The single-rat test is unsuitable for clinical purposes. By increasing the number of test animals, however, any desired degree of accuracy can be obtained.

I wish to express my thanks to Dr. J. A. Fraser-Roberts for his advice on the statistical analysis and to Mr. D. M. Stern for his kindness in providing test material.

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Medical Memoranda

An Unusual Rectal Injury

The following rectal injury would appear to be so unusual as to merit recording in some detail.

CASE REPORT

A man aged 24 was admitted to hospital on November 5, 1953, complaining of severe abdominal pain of twelve hours' duration. He gave a history of a similar attack of severe pain six weeks previously, and stated that over the past ten years he had been subject to attacks of abdominal pain, lasting two to three hours, and sited around the umbilical region. The evening before admission he began to have diarrhoea, and passed both bright and dark red blood per rectum. Vomiting had occurred on the morning of admission. There was no previous history of melaena, and the bowels had been opened regularly each day.

On examination he was pale and collapsed; pulse 130. The abdomen was distended, with generalized tenderness and guarding, most pronounced in the lower half. The bowel sounds were absent; no tumour could be palpated. Per rectum, bright red blood was present in the anal canal. There was much tenderness, and a "doughy" feeling above the prostate which could have been caused by an intussception, but exact palpation was not possible because of the great tenderness. Proctoscopy revealed copious fresh and altered blood, and a continual stream of faecal matter which made it impossible to visualize the anal canal or lower rectum.

Operation through a right lower paramedian incision, performed three hours after admission, revealed an extensive retroperitoneal extravasation of blood but no evidence of an intraperitoneal injury, though blood-stained fluid was present, together with considerable bruising of the mesentery of the small bowel in the region of the sacral promontory. The small and the large bowel were normal. In the absence of an intraperitoneal lesion the wound was closed. The rectum was again examined, and, now that the patient was anaesthetized and relaxed, a circular tear the size of a two-shilling piece was felt in the anterior rectal wall above the prostate. Blood clot and fluid faeces were present, and a considerable amount of bleeding was coming from this laceration. There was no evidence of injury to the anal or perianal regions, and the sphincter was of normal tone. It was now clear that this was a traumatic injury. A rubber tube was passed up the anal canal, through the laceration in the rectal wall, and into the perirectal tissues. Immediately there was a copious discharge of altered blood, together with a quantity of turbid and offensive fluid. The tube was sutured to the anal margin to keep it in position. A left inguinal colostomy was established and opened immediately.

Post-operatively the treatment was continuous gastric suction, intravenous fluids, penicillin, and streptomycin. In all, 5 pints (3.7 litres) of blood was given. The discharge from the rectal tube was copious for some days, and it was left in position for a week. Recovery was uneventful, and the patient left hospital nineteen days after admission. The laceration in the rectal wall could still be felt, but healing

was proceeding satisfactorily. He was readmitted a month later for closure of the colostomy. By now the rectal wound had healed. He was discharged after ten days with a normal bowel action; when seen for follow-up purposes six weeks later all was well.

COMMENT

The question now arose of how this injury had been inflicted. Many possible causes were considered, including the "compressed air" joke and some unnatural sex act, but none seemed to fit this particular case. When the patient was approached he first said he was standing too near a firework, and it had gone off while he was in a stooping position. When told this could not be so and he would have to tell the truth, he gave the following astounding explanation. For domestic reasons he had become unhappy and morose, and on the evening of November 4 he decided to explode a firework up his seat. He accordingly fashioned a narrow tube, using cartridge paper, and with the aid of a pencil introduced one end of this tube, approximately 6 inches (15 cm.) in length, into his rectum. He then placed a lighted firework into the end of the tube projecting out of his anus, with the result that a hole was blown through the anterior rectal wall. This escapade had taken place the evening previous to admission.

At first this story was accepted with reservations. What, for instance, happened to the firework—no charred bits were detected. Could a paper tube, even of stiff paper, be introduced into the anus against the action of the sphincter, and would there not have been some signs of singeing at least around the anal regions? However, there appeared to be no other reasonable explanation. He was referred to a psychiatrist, who stated there was no doubt this was indeed the true sequence of events.

The history in this case was grossly misleading, but had, of course, been made so deliberately. Had there been any suspicion of trauma to the rectum, examination under general anaesthesia would have been the first step.

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Ruptured Infected Urachal Cyst

This condition is rare enough to warrant the report of a single case.

CASE REPORT

A boy aged 16 was sent into hospital as an emergency case. The accompanying note from his general practitioner stated "appendicitis." The patient said he had always been perfectly well until ten days previously, when he noticed that about half-way through the act of micturition he developed lower abdominal pain of such severity that he was obliged to terminate the flow. This symptom persisted for four or five days, during which he was seen at another hospital; no abnormality, however, could be found. On the day before his admission the lower abdominal pain had become much more severe and was now constant. Micturition was still painful and there had been some diarrhoea. He had vomited several times.

On admission he was obviously ill, with earthen complexion and coated tongue. His temperature was 99° F. (37.2° C.) and pulse rate 92. The abdomen did not move on respiration and there was generalized muscle-guarding with rigidity across the hypogastrium. Tenderness appeared to be maximal in the right iliac fossa. Rectal examination revealed marked tenderness in the recto-vesical pouch. There were no bowel sounds on auscultation of the abdomen.

The history was a little strange and not typical of acute appendicitis. Clearly, however, he had peritonitis, and this appeared to originate from some condition in the pelvis. A pre-operative diagnosis of a perforated pelvic appendix was therefore made—on the grounds that "common things are commonest."

The abdomen was opened through a gridiron incision. There was much pus in the peritoneal cavity, but the appendix was normal. Further palpation revealed an extraperitoneal mass overlying the fundus of the bladder, with a finger-like prolongation extending upwards in the midline along the deep aspect of the anterior abdominal wall. The appendix was removed. A lower right paramedian incision was then made and the previous findings were confirmed. Omentum was adherent to the mass, and when this was separated an abscess cavity the size of a plum was opened from which pus and debris escaped. The situation of the mass and the midline upward prolongation from it made the diagnosis obvious: this was a ruptured infected urachal cyst. The pus was cleared away from the peritoneum and a drainage tube inserted through the gridiron incision to the abscess cavity. Both incisions were then closed. A cystoscope was passed and a little dimple, with a collar of mucosa around it, was seen in the roof of the bladder. There was no sign of any inflammatory process in the bladder.

Post-operative progress was satisfactory, both wounds being well healed by the tenth day. A specimen of pus from the abscess cavity contained mucoid material and numerous pus cells. No organisms were seen and no growth could be obtained on culture. A cystogram showed a normal bladder outline. Seven weeks after the operation the patient was in good health and symptom-free. No abnormality was detected on examination of his abdomen and rectum.

COMMENT

This subject was well reviewed by Brodie (1945), who included a survey of the literature up to that time. Apparently the earliest recorded case is attributed to Cabral in 1550. Urachal cysts are likely to be present in one of two ways: (1) the cyst may become large enough to cause pressure symptoms or to be discovered on routine examination of the abdomen; or (2) it may become infected and later rupture into the bladder, bowel, or peritoneal cavity, or a fistula may develop along the urachal track to the umbilicus. Other reported complications include tuberculous infection, calculus formation, and neoplastic change. Kantor (1939) believes that infection reaches the cyst by direct extension from the bladder along a narrow channel which later becomes obliterated by the inflammatory process. Others favour lymphatic or haematogenous routes. It is interesting to note that in a number of cases, including the present one, no organism has been cultured from the cyst contents.

All authors are not agreed on the method of treatment of the ruptured infected cyst. Some favour immediate excision and others preliminary drainage followed later by excision. A few suggest curettage and irrigation with silver nitrate. Callanan (1951) and Everett (1942) each report a case in which a ruptured infected urachal cyst was excised, together with adjacent bladder wall, at an emergency operation. In both cases histological examination showed the lining membrane of the cyst to be almost completely destroyed. Baldwin (1912), operating for incisional hernia four months after draining an infected urachal cyst, found no trace of the cyst. Kantor (1939) describes a case successfully treated by incision and drainage, and Gross (1953) reports five cases similarly treated. In four of Gross's patients no further treatment was necessary, but in the fifth a recurrence necessitated excision of the mass. It would seem reasonable, therefore, to treat these cases by simple drainage in the first instance. Excision would then be indicated only if there were further attacks of inflammation, if a fistula developed, or if a mass persisted in the abdomen. The likelihood is that the cyst cavity becomes obliterated after a bout of inflammation severe enough to cause its rupture.

I would like to thank Mr. W. M. Beattie for permission to report this case.

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Reviews

JUVENILE DELINQUENCY

Police Work with Juveniles. By J. P. Kenney and D. G. Pursuit. Foreword by August Vollmer. (Pp. 371+xxi. 55s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1954.

Growing Up in the City: A Study of Juvenile Delinquency in an Urban Neighbourhood. By John Barron Mays, M.A. (Pp. 216+ix. 17s. 6d.) Liverpool: University Press. 1954.

It has been estimated that in the United States "from 50 to 75% of a police agency's work directly or indirectly affects youth." Doubtless the same is true in most other civilized communities. Yet in the standard works dealing with the functions of the police the problems of juvenile delinquency rarely occupy more than a few pages. Professor Kenney and Mr. Pursuit have sought to fill this gap by publishing a systematic survey of the whole subject from the standpoint of the practical administrator. Their project was in part a direct result of the policy of "professionalizing the services of law enforcement," sponsored by J. Edgar Hoover, the Director of the Federal Bureau of Investigation, who (we are told) has also "given leadership in improving police relations with juveniles." The outcome is a well-documented manual intended to assist police officers in building up an "up-to-date and progressive juvenile programme."

The book is divided into three main parts. Part I opens with a brief review of police responsibilities in regard to "the control and prevention of anti-social youth activities and of any conditions that may be conducive thereto," and then describes in practical detail the establishment and administration of a local police department concerned with juvenile offenders, illustrated by a number of charts showing the ideal police organization required for districts of specified area and population. This is supplemented by separate chapters on the selection and training of policemen and policewomen for juvenile work; methods of prevention and supervision so far as they fall within the scope of the police; the compilation of records; and the maintenance of sound public relations through the Press, through radio and television, and by speeches or discussions at local clubs and the like.

Part II is concerned with "individualizing the police approach." It begins with a short theoretical account, emphasizing the causal complexity of the problem, and presenting a simplified synopsis of the commoner factors making for delinquency, as disclosed by the researches of Healy, Bronner, Sheldon, Glueck, and others. The practical sections discuss the principles of individual and social investigations; methods of interviewing and carrying out case studies; the disposal of juvenile offenders after referral to courts, local education authorities, or the like; and finally the establishment of helpful relations between the police and the parents in cases where drastic measures appear unnecessary.

Part III deals with "team work for delinquency control and prevention." It reviews the chief functions of the school, the Church, the juvenile court, the probation service, and the commoner agencies for social welfare, and concludes by advocating a systematic "community plan" for co-ordinating the work of these various bodies in every area, and urging that the police should take an active and sympathetic part in helping to organize it. The volume is compiled primarily with American problems and conditions in mind, but should prove valuable as a work of reference for all engaged in combating juvenile crime.

Mr. Mays's book describes one of the most instructive inquiries carried out in this country on the causes and treatment of juvenile crime. His investigation was started five years ago, while delinquency was still increasing. As warden of a University Settlement situated in one of the worst slums of Liverpool, his first-hand knowledge and experience enabled him to make an intensive study of social and environmental factors, which, as he points out, have so often been overlooked. The outstanding features of the district were, according to his figures, poverty, bad housing, casual employment, educational backwardness among the children, a strange admixture of races, and a clash of cultures and religious beliefs. In areas such as this, so he maintains, delinquency almost inevitably becomes a social tradition.

Detailed evidence for his view is provided by the case histories of eighty lads, all members of a local youth club, who were observed and interviewed over a period of several months. Thirty were known to have been convicted of larceny or the like; another twenty-two eventually confessed to similar offences. Two types of offender seemed discernible—the "criminals" (that is, habitual offenders who form the leaders and set the tone) and the "delinquents" (that is, occasional or temporary offenders who merely conform to the codes and customs of those around them). The story of their daily lives, pieced together as their confidence was gained, suggests that with both groups the lawless misconduct was a symptom not so much of maladjustment as of adjustment to a particular subculture which happened to be in conflict with the general culture of the community as a whole. And the author's main conclusion is that "juvenile delinquency is just one aspect of the general behaviour pattern that obtains in under-privileged neighbourhoods."

In the light of his results he appends a series of practical recommendations. Instead of psychiatric treatment at clinics, "often lengthy and nearly always costly," he pleads for a better co-ordination of existing social services, and proposes the appointment of "special family welfare officers" who would help parents and teachers to cope with incipient cases before more drastic measures became necessary.

CYRIL BURT.

VIRUS RESEARCH

Advances in Virus Research. Volume II. Edited by Kenneth M. Smith and Max A. Lauffer. (Pp. 313+x; illustrated. $7.) New York: Academic Press, Inc. London: Academic Books Ltd. 1954.

The editors' aim is to publish in these annual volumes critical review articles which in course of time will provide the material from which to synthesize one's views on virology as a whole. An attempt is made to achieve a balance in each volume, and Volume II fully maintains the high standard set by its predecessor. It begins with two articles on plant viruses: one on the inheritance of resistance to virus disease by Francis O. Holmes, and the other by F. C. Bawden, of Rothamsted, dealing with inhibitors of plant viruses. Both are subjects of the greatest importance, and those who work with animal viruses will be particularly interested to read what Bawden has to say about the chemotherapy of virus disease of plants, and in particular on the possible future developments in this field of research. Animal viruses provide the theme in the next two articles, in one of which von Magnus, of Copenhagen, discusses the production of incomplete forms of influenza virus and their significance, while in the other W. Wilbur Ackermann and Thomas Francis, jun., consider the development in isolated animal tissues. If one were to select one article from among the eight in this volume for particular mention it would probably be that by Ackermann and Francis. It is delightfully lucid and logical, and the conclusions drawn from the information presented strike one as very sound; incidentally, there is no reference to an eclipse phase in the development of the viruses under consideration. Ernest Pollard contributes a valuable section on the use of ionizing radiation in virus research and C. A. Knight writes on the chemical constitution of viruses. The book concludes with articles on the electron microscopy of viruses by Robley C. Williams and one by Lauffer and Bendet on the important question of the hydration of viruses.

In this brief review it has been possible to do little more than indicate the contents of this work, but one might in conclusion congratulate the editors and the authors on having made a valuable contribution to the literature of virology.

S. P. BEDSON.

MEDICINE IN WAR

Medical History of the Second World War—Army Medical Services. Administration, Volume II. Edited by F. A. E. Crewe, F.R.S. (Pp. 564+xxvi; illustrated. 65s.) London: H.M. Stationery Office. 1955.

Exactly a hundred years ago, in the Crimea, Florence Nightingale laid the foundations for an efficient Army Nursing Service, and at the same time closely and critically observed the almost total lack of efficient hygienic and sanitary precautions in the Army. It is common knowledge that she gave years of her life to develop the former and to correct the latter. These facts inevitably came to mind when perusing this well-produced volume dealing with the administration of the Army Medical Services during the war of 1939–45. How it would have rejoiced Miss Nightingale's heart to read this book, for in it she would see brought to fruition all, and more than all, she strove for. Various sections deal respectively with the administration of nursing, hygiene, dental services, pathology, blood transfusion, the Auxiliary Territorial Medical Service, psychiatry, medical research, ophthalmology, and radiology. The section on hygiene is a remarkably comprehensive exposition of preventive medicine under war conditions, and should prove a most useful source of reference for all future workers in this field. Another section of special interest is that dealing with the gradual development of the medical provision for the large numbers of women in the Auxiliary Territorial Service; the many special problems consequent on the enlistment of such large numbers of women are here described and their solution outlined.

Though the material for this book came from a number of varied sources the editor has skilfully contrived to bring about a harmony and balance in the whole volume. To avoid the constant repetition of the names of institutions and officials frequent use is made throughout the book of the initials of the official designations of the various bodies referred to. The editor has wisely helped the reader by inserting a list of abbreviations, which will also prevent laymen making a mistake over the significance of M.C.C., M.F.H., or even T.O.T. This volume worthily upholds the high standard of production consistently reached by the volumes of this remarkable series.

ZACHARY COPE.

THE RORSCHACH TEST

Le Test de Rorschach et la Personnalité Epileptique. By J. Delay, P. Pichot, T. Lempérière, and J. Perse. (Pp. 218. 1,000 fr.) Paris: Presses Universitaires de France. 1955.

This book, which assumes familiarity with the Rorschach test and terminology, is in three parts. The first puts forward evidence that epileptics have a certain personality type. The authors admit that there are contradictions about its characteristics, but do not seriously question its existence.

The second part reviews nearly 80 studies of epileptics with the use of the Rorschach test. The authors conclude that it is a valid instrument for exploring personality, but criticize previous work because of too few subjects, lack of relation to intellectual level, the use of in-patients only, poor statistical techniques, and failure to differentiate between epilepsies of different aetiology.

The third part describes an investigation of 50 epileptics. Their Rorschach records were analysed into two unrelated "dimensions": the presence of various organic and epileptic Rorschach "signs" or their absence; and an extensive profile with more than 15 responses with emphasis on colour responses, or the reverse. Idiopathic epileptics, both with foci in the temporal lobes and elsewhere, were found to have constricted records; post-traumatics and those with psychomotor temporal lobe attacks, the reverse.

However, the study is open to some of the authors' own criticisms. The 50 subjects have an age range from 15 to 50, the sexes are not balanced, and nearly half have unstated foci. The frequency of fits is not considered, nor the duration of the disability, though this is stated, and ranges from less than a year (three cases) to more than 20 years (eight cases). The authors limited themselves to showing the validity of certain Rorschach signs, but make no conclusions on whether the personalities of epileptics show more than certain broad similarities revealed in their "dimensions." They do not state their opinion of the reliability of the test in diagnosing epilepsy, particularly in relation to the E.E.G., and they have not considered in what way the protocols of their temporal lobe epileptics differ from those of schizophrenics, though the clinical impression and symptoms are often similar.

CLIFFORD JACKSON.

DIAGNOSTIC ELECTROCARDIOGRAPHY

Diagnostic Electrocardiographique. By André Jouve, Jacques Senez, and Jean Pierron, with eleven collaborators. Preface by Professor Ch. Laubry. 2nd edition. (Pp. 448; 242 figures. 4,000 fr.) Paris: Masson et Cie. 1954.

The new edition of this book on diagnostic electrocardiography appears some eight years after the first. As the authors remark, so much has been found out since then that a completely new presentation is needed, although the general plan of the work remains the same as before. The first of the four sections deals with the anatomy and physiology and general principles. The authors have made much use of the vector interpretation of cardiograms. The reader will meet this right away. This is entirely as it should be: here is the true point of departure. The authors point out that the empirical indications given by the practice of cardiography are much better understood than the theoretical bases on which this knowledge is founded. It really made very little difference 25 years or so ago when, for example, right ventricular curves became left, and vice versa. The vectorial interpretation serves to integrate the vast mass of information gathered during the last 50 years, so that one gets a complete view of the cardiac electrical field and an interpretation instead of a mnemonic description. One may say at once that all this is carried out with a clarity and economy of expression that is a pleasure to read; it is not formidable at all.

The second section deals with the practical application of these ideas, as regards auricular and ventricular overload, infarcts, and so forth; the third section, with time relationships and so the arrhythmias and delays in conduction. Finally there is a section dealing with the clinical application of cardiography to various morbid states, mostly primarily extracardiac.

The illustrations for the most part are clear. It is a pity some of the vectorgrams are smudgy, as are also some of the cardiograms. They were better all shown as line drawings. They hardly reach the level of perfection that most American books now attain, but there are not too many curves. The lavish presentation of redundant specimens is avoided. The print is clear and the paper good. Each chapter has numerous references. There are but minor defects; the reading matter is so clear, well expressed, and well arranged that one can give it very high praise.

TERENCE EAST.

Occupational and Related Dermatoses is the third of a series of such bulletins published by the U.S. Public Health Service. It contains 1,170 abstracts of articles on occupational skin diseases from American and foreign journals. These abstracts are grouped alphabetically under the factors causing the complaint, and there is a general contents list but no index. The bulletin covers the period from July, 1943, to December, 1953, and should prove very useful in any search for information on contact dermatoses. The bulletin, which is Public Health Service Publication No. 364, can be obtained from the Superintendent of Documents, Government Printing Office, Washington 25, D.C., U.S.A., for 65 cents.

BRITISH MEDICAL JOURNAL
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SAFER NUCLEI

The long-term effects which may be produced in large populations by continued exposure to ionizing radiations have been widely discussed since the hydrogen bomb test at Bikini Atoll in March, 1954. The problem arises also, if in lesser degree, from the treatment of the radioactive materials to be produced in increasing quantities by nuclear reactors in power stations, and it was discussed in this context at the recent Geneva conference on the peaceful uses of atomic energy. The prevention of damage by radiation depends partly on the safe design and operation of nuclear power stations, and partly on the safe disposal of the radio-isotopes which will be produced as fission products. Another aspect is the extent to which increased general exposure to radiation should be tolerated. Finally, there is the question of what harm may be expected in the event of accidents.

The first point—that of safe design and operation—could perhaps be sufficiently met by the adoption of agreed codes of practice. In a properly designed station the leakage of radioactive materials should be negligible by any standards. But in the long run nuclear power stations will be operated by Ruritania as well as by countries from whom efficient control may be taken for granted, and there will therefore be a need for agreement. The second point—the disposal of radioactive materials—was expressed in quantitative terms by E. Glueckauf (U.K.) on the basis of an ultimate world consumption of fissile materials at the rate of 1,000 tons a year, and the formation of radioactive fission products from them at the same rate. On this basis, and if fission products were stored for only one year before discharge (much less than would be seriously contemplated), and if all the material discharged were assumed to be uniformly mixed in the oceans, the eventual build-up of radioactivity would be about equal to that now contributed by the natural radioactive potassium present in sea water. The comparison is incomplete in several ways. But in conjunction with another estimate, quoted by Sir John Cockcroft, that the consumption of fissile materials may amount to between 2,000 and 3,000 tons a year by A.D. 2000, it does suggest that the amount and manner of discharge will need to be seriously considered. The onus is thus placed on biologists, and especially geneticists, to provide the information on which long-term standards can be based.

A recommendation of the International Commission on Radiological Protection states that large populations should not be exposed to a dosage exceeding 0.03 r a week—that is, to one-tenth of the level for workers liable to be exposed to radiations in their jobs. This approximates to a dosage of 50 r per generation of 30 years, the level which has been found in a variety of organisms to double the mutation rate. However, as W. Binks, the secretary of the Commission, pointed out at the conference, "large populations" should not for this purpose exceed 10% of the whole population; or alternatively a bigger reduction factor should be used. In a general review of the genetics T. C. Carter (U.K.) quoted A. H. Sturtevant as saying that "no scientist interested in exact quantitative discussion would touch the subject were it not that its social significance leaves us no alternative," and summarized his own analysis of the application of mouse data to man as leading to a "colossal" (thousandfold) uncertainty, though possibly still not big enough to include the truth. To say that the answer lies in research is to state the obvious. But it has not been obvious that the obtaining of more directly applicable data could reasonably be regarded as practicable. Carter's proposal is for research at three levels, undertaken on an international scale and taking ten years or more to complete. Studies of mutations as such should be spread over many types of cells in many different organisms, including vertebrates, and should include "studies of the effects of ionizing radiations when administered at very low dose rates over a long period"; the point is to determine whether the risk increases additively. Secondly, Carter pointed out that research on population genetics has lagged far behind theory, and he proposed a large programme of research to set this to rights. Thirdly—and this is perhaps his most interesting point—he proposed a direct attempt to determine the relation between radiation exposure and mutation rate by making use of the appreciably higher background radiation in granitic areas of Great Britain and Scandinavia compared with that in granite-free areas of the same countries. He thought it might be possible "to make estimates of the mutation rates of a few clear-cut autosomal dominant or sex-linked recessive conditions (e.g., achondroplasia, epiloia, haemophilia) with sufficient accuracy to enable us to set useful fiducial limits to the mutation-rate-doubling radiation dose in man." As well as physical and medical data, we should need also to know about population movements during considerable periods of time. Such points will no

doubt be discussed at the international conference which J. F. Loutit (U.K.) announced later is to be held by the Medical Research Council at the Atomic Energy Research Establishment, Harwell, on September 19 and 20. It should serve a useful purpose in calling attention to the technical possibilities of investigations, and will be a useful preliminary to making them. Whether this goes far enough may be another matter. If international standards of safe practice are to be achieved, there may be a case for international co-ordination at the research stage. The functions of the World Health Organization were defined by P. Derolle at the Geneva conference as the bringing together of research workers and the dissemination of information; it did not itself do research. Hence the suggestion revived by R. Sievert (Sweden) that a new international body should be established to cover "the general radiation problems of the world." His proposed body "would be empowered to promote essential research in its field and to organize continuous general supervision of the radiation level of the world." There will be support from doctors for his further specification that "it should have a high standard of independence and sufficient means, and should not be under restrictions on publication of its findings. These should be reported periodically . . . with summaries that would be understood even by the man in the street." The need is not only for facts; their collection and interpretation must be evidently impartial.

On the assumption that standards will have been determined, the kind of scheme that might be adopted for the disposal and use of radioactive materials was suggested by Glueckauf's discussion of the subject. After initial concentration he envisages the removal of the troublesome long-lived radio-isotopes strontium-90 and caesium-137, and their use for 50 years as sources of radiation or heat. Bulk storage of the residue for thirteen years would be followed by the recovery, for profit, of certain rare metals then of much reduced activity and the permanent storage or disposal of what was left. On this basis Glueckauf concluded that the final product would have an activity only one-thousandth of that of the radioactive potassium in the oceans, and could be disposed of safely, possibly in plastic containers sunk in deep water. However, the separated isotopes of strontium and caesium would remain highly active for a millennium, and would require to be otherwise disposed of, possibly by storage in a solid form from which the radioactive components could not be dissolved. A final question of public health interest will be to ensure the proper control of the large quantities of radioactive materials which will be in use in industry as well as medicine. There must be no possibility of their finding their way via rubbish dump to playing field, as could conceivably happen.

The remaining question is about the extent of local hazard to be expected if a nuclear reactor misbehaves. J. R. Dietrich (U.S.A.) described experiments in which a reactor had been deliberately provoked to behaviour which, if photographically dramatic, was found to be unalarming radiologically. C. R. McCullough (U.S.A.) gave a more highly coloured rendering of the type of disturbance which might be expected from an accident on a larger scale; the evacuation of a large city or the abandoning of a major watershed might be necessary. W. G. Marley and T. M. Fry (U.K.) concluded that, under certain conditions, it would be enough to evacuate temporarily from a narrow sector extending 5.7 kilometres (3½ miles) down wind, and to be prepared for the possibility of seriously contaminated milk from pastures up to 20 kilometres (12 miles) away. Apart from occupational hazards, which will no doubt continue, as now, to be adequately looked after, the most important questions of public health remain those associated with the long-term exposure of large populations to small increases in radiation, and it is well that these have begun to be seriously considered.

MITRAL VALVOTOMY

The success of mitral valvotomy in relieving the symptoms of severe mitral stenosis is now well recognized: earlier reports showed that nearly three-quarters of patients, many of them severely incapacitated, were restored to normal health and activity.[1,2] It is too soon yet to assess the duration of the results of operation, but recent papers suggest that in most patients the improvement is maintained up to five years. In the opening pages of the *Journal* this week Mr. W. P. Cleland and his colleagues report their results in 75 patients submitted to mitral valvotomy; they have followed up 56 of them for periods ranging from six months to three years. One year after operation the results were good in 26 out of 41 patients, and after two years no deterioration had occurred in 11 out of 16 patients; 3 had improved further and 2 were worse. In a large series of 500 cases followed up for an average period of twenty-two months and in some cases for five years, L. B. Ellis and D. E. Harken[3] found that 77% of patients were improved, and that only 31 of those patients who had shown improvement six months after operation had deteriorated. The question whether stenosis of the valve occurs again and is responsible for this late deterioration cannot yet be answered. Paul Wood[4] thought that it had occurred in 5% of his

patients, but most other reports state that it is rare.[5] It seems more likely that late deterioration is caused by an inadequate valvotomy or simple dilatation of the valve opening, or by other factors such as the production of mitral incompetence at operation, active rheumatism, myocardial disease, or associated aortic valve disease.

Analysis of the results of mitral valvotomy carried out in many different centres shows that a good result is obtained in about 70% of cases. The improvement is largely subjective; effort tolerance increases, while attacks of nocturnal dyspnoea, "bronchitis," and haemoptysis disappear or become much less frequent. This marked improvement in symptoms is in most cases not accompanied by any objective evidence of improvement, the heart size remaining unchanged or increasing, the auscultatory signs showing little change, and the clinical and radiological evidence of pulmonary hypertension being the same as before operation. There is the same discrepancy between subjective improvement and the results of post-operative cardiac catheterization and lung function studies. The pulmonary artery pressure often falls soon after operation and may continue to fall over the following six months,[6] but there is no relationship between changes in pulmonary artery pressure and cardiac output and the improvement in breathing. Because of this discrepancy between subjective and objective improvement it has been suggested that in many cases the improvement is psychogenic.[7] In a small number of cases a simple thoracotomy or unsuccessful valvotomy has been followed by a decrease in effort dyspnoea, but this improvement is usually of short duration and does not compare with the long-lasting benefit of a successful valvotomy. The probable explanation for the striking improvement in dyspnoea in spite of the absence of clinical, radiological, or catheter evidence of change is given by the work of G. W. Hayward.[8] He showed that the increased rigidity of the lung, which is largely responsible for the dyspnoea in severe mitral stenosis, is caused by interstitial oedema of the lung due to the increase in pulmonary capillary pressure, which may exceed the effective plasma osmotic pressure. After a successful valvotomy the lung becomes less rigid, and the striking increase in rigidity on effort which occurred before operation is abolished.[9] These changes are attributable to the fall in left atrial and pulmonary capillary pressure produced by operation and will occur whether or not there is any change in the pulmonary artery pressure or heart size. The *x*-ray appearance of the lung in mitral stenosis is largely influenced by the degree of pulmonary hypertension and the condition of the pulmonary arteries, and will not show any of these changes in the pulmonary capillary circulation.

If good results are to be obtained by mitral valvotomy, careful selection of patients is essential. Mitral stenosis is not necessarily progressive, and only a minority of patients with little or no cardiac enlargement ever develop symptoms,[10] so that operation is unnecessary in those cases. The chief indication for operation is dyspnoea which is disabling and progressive and which can be shown to be caused chiefly by the mechanical obstruction in the circulation at the mitral valve. Dyspnoea is a symptom which is notoriously difficult to assess, and many patients with minimal valve damage are dyspnoeic either because unwarranted limitation of their physical activities has caused a cardiac neurosis or because some other factor is present, such as obesity, chest infection, or anaemia. In these cases objective evidence of pulmonary hypertension is absent and operation is contraindicated. In most cases with marked obstruction at the mitral valve the disability is beyond doubt, particularly if it is accompanied by orthopnoea or paroxysmal dyspnoea and there is in addition evidence of pulmonary hypertension, as shown by the clinical signs of right ventricular hypertrophy and the radiological changes in the size of the right ventricle and in the branches of the pulmonary artery. More information on the severity and effects of mitral stenosis is provided by proper clinical and radiological examination of the patient than by cardiac catheterization, and an interesting development of the last few years has been the growing appreciation, at least in Britain, of the amount of information about the state of the mitral valve which can be obtained by simple clinical methods.[4]

Many problems still remain to be solved. The relative importance of myocardial damage and valvular obstruction in causing symptoms is not always easy to establish, though if the heart muscle is damaged the heart is usually larger, auricular fibrillation is more common, and evidence of right ventricular hypertrophy is less marked, while dyspnoea is more variable in severity and there are often relatively asymptomatic periods.[11] Peripheral emboli at the time of operation occurred in 42 of the 500 patients reported by Ellis and Harken[3] in spite of

[1] Bland, E. F., *Circulation* (*N.Y.*), 1952, **5**, 290.
[2] Baker, C., Brock, R. C., Campbell, M., and Wood, P., *British Medical Journal*, 1952, **1**, 1043.
[3] Ellis, L. B., and Harken, D. E., *Circulation* (*N.Y.*), 1955, **11**, 637.
[4] Wood, P., *British Medical Journal*, 1954, **1**, 1051 and 1113.
[5] Glover, R. P., Davila, J. C., O'Neill, T. J. E., and Janton, O. H., *Circulation* (*N.Y.*), 1955, **11**, 14.
[6] Munnell, E. R., and Lam, C. R., ibid., 1951, **4**, 321.
[7] Soloff, L. A., and Zatuchni, J., *J. Amer. med. Ass.*, 1954, **154**, 673.
[8] Hayward, G. W., *British Medical Journal*, 1955, **1**, 1361.
[9] —— and Knott, J. M. S., *Brit. Heart J.*, 1955, **17**, 303.
[10] Grant, R. T., *Heart*, 1933, **6**, 275.
[11] Harvey, R. M., *et al.*, *Circulation* (*N.Y.*), 1955, **11**, 531.
[12] Daley, R., Mattingly, T. W., Holt, C. L., Bland, E. S., and White, T. D., *Amer. Heart J.*, 1951, **42**, 566.

the measures taken to minimize the risk; 19 of these cases were fatal. Operative emboli occurred most often if the valve was calcified and if the patient had severe congestive failure and auricular fibrillation. In this series and that of Cleland *et al.* it seems that the risk of the patients developing a late peripheral embolism is considerably decreased by operation, but it has yet to be decided whether a history of embolism, without other symptoms, is a sufficient indication for operation. Second or multiple attacks of embolism are common,[12] and if in addition there are other symptoms and signs such as dyspnoea and auricular fibrillation operation should be carried out both to relieve symptoms and to lessen the risk of a subsequent embolism.

If the cases have been carefully selected, the result and safety of the operation will be determined by the skill and experience of the surgeon. Increasing experience of valvotomy results in a higher proportion of effective operations with a decreased risk of later deterioration of the patients and a lower operative mortality.[3] The timing of the operation is important, and it should be carried out when disability is established and progressive but before the patient develops serious congestive failure; yet even in these bad-risk cases good results can often be obtained.[2]

HOSPITAL ADMINISTRATION IN N.H.S.

The recent correspondence in *The Times* on hospital administrators and doctors brings to light a state of affairs that has been worrying for some time many medical men working in the vast hospital service of this country. It is not for us to judge whether the incident which prompted Mr. D. Le Vay to write the first letter in this correspondence showed wisdom of action on the part of the consultant and his registrar. The consultant was satisfied with the arrangements for the care of patients during the absence of both of them. They both wanted to widen their professional knowledge by attending a conference, to the ultimate benefit of their patients and the hospital service in which they were working. From the medical standpoint these seemed to be sufficient reasons. From the administrative standpoint the action was that of "a registrar who, contrary to orders, deserts his post for a few days," writes the Secretary of the Institute of Hospital Administrators. The penalty for disobedience and desertion is instant dismissal, and that, for the administrator, is that. Whether the patients in the hospital from which the registrar is dismissed suffer because of the discontinuity in treatment thus brought about, and because of the loss of this man's professional skill, appears to be of less importance than the correct execution of the administrative rule of law, almost military in its severity. If the patients suffered because of the doctors' actions the doctors would find no harsher judges than their own colleagues, but so far no evidence has been brought forward to show that they did. The fact that medical men were serving on the board—representing the administrator—is beside the point: as Mr. D. H. Patey observes "in the present context [they] are administrators."

Clinical responsibility and administrative responsibility are two separate things. It is difficult for clinician and administrator to understand each other's points of view. The one's principal concern is with human beings; the other's, with the mechanism of a service. As Mr. Le Vay put it: "The relation between doctor and patient is a very special one and it ought not to be exposed to (such) stresses if the quality of clinical work is to be maintained." The sick person is very conscious of this special relationship, and his recovery depends to a great extent upon it. The healthy administrator, isolated from the clinical scene, thinks the clinician makes too much of this relationship, and in moments of irritation likes to accuse doctors of acting like prima donnas. The doctor looks upon the hospital service as something which should provide optimum conditions for the treatment of sick persons and, to this end, for acquiring and improving professional experience and skills. The administrator looks upon it as an inefficiently conducted industry, and if an employee—and that is what the doctor working in the hospital service is—does not obey the exact letter of the regulations then he gets the sack. The doctor, having full clinical responsibility, is disquieted to find that the administrator has the power—the power to interrupt his work, to prevent his advancement, to injure his career. He feels increasingly uneasy at what appears to him a divorce between power and responsibility. As Dr. W. A. Bourne so well puts it: "All threads pass through the hands of administrators who interpret facts and regulations to a regional board of part-time members largely occupied in other directions, or state the board's policy to smaller committees throughout the region." No one who has the welfare of the hospital service at heart can fail to be dismayed by Dr. Bourne's disclosure of the fact that he was "asked to agree to surrender a hospital ward to another specialty *to save an official of the board from personal embarrassment . . .*" (our italics); and that for similar reasons the advice of professional appointments committees was overruled. What an abuse of power!

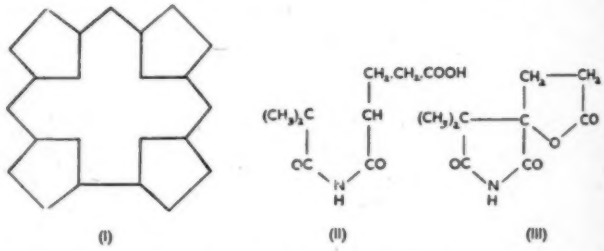
[1] *Report of the Committee on the Internal Administration of Hospitals*, H.M.S.O., 1954. See *British Medical Journal Supplement*, October 2, 1954, p. 133.

From his position as chairman of the Central Consultants and Specialists Committee of the B.M.A. Dr. T. Rowland Hill has given his authoritative endorsement to the truth of the picture Dr. Bourne paints. Dr. Hill makes it clear that in his view the relationship between hospital administrators and the medical staff of the hospitals is on the whole unsatisfactory: "There are too many bad patches throughout this Service. . . ." In *The Times* correspondence there are complaints of "a tight hierarchical system," "the present cast iron system," "the struggle which is being waged with increasing intensity between the administrators and the medical and nursing staffs of our hospitals," "excessive centralization of authority." No doubt there have been faults on both sides. We know that administration is necessary, and that many able and hard-working administrators are playing an indispensable part in running the hospital service of the N.H.S., often in circumstances of great difficulty. Yet some of them appear to act as though administration were an end in itself and not just a means towards the end for which the hospital service exists—the care of sick persons by skilled professional men and women. The present distressing state of affairs was forecast often enough in these columns before the N.H.S. came into operation, and the present discontents are not surprising. But they must be met and solved if the public is to receive the kind of service that can be given only if doctors are proud and content to serve in it, and are treated as responsible partners in a great humane enterprise instead of as servants subject to a multitude of petty restrictions and instant dismissal. The profession as a whole will surely support the plea of Dr. Hill that there is a case for an immediate inquiry at the highest level into hospital organization, and the report on many features of it completed last year by a Central Health Services Council committee would serve as one starting-point.[1] His plea is cogently supported by Mr. Herbert G. Tanner, who speaks with the authority of six years' experience as chairman of the South-west Regional Board. The sooner it is carried out the better.

STRUCTURE OF VITAMIN B_{12}

The story of vitamin B_{12} goes back nearly thirty years to 1926, when Minot and Murphy discovered that liver is curative in pernicious anaemia. But progress in isolating an anti-anaemic principle from it was hampered by the lack of an experimental animal or a biological technique for assaying the haemopoietic potency of liver extracts. Twenty-one years were to elapse before a microbiological method was perfected for assaying the haemopoietic activity of liver. It was in 1947 that M. S. Shorb observed there was a linear relation between the amount of growth factor for *Lactobacillus lactis* Dorner in liver extracts and the potency of the latter for curing patients who had relapsed in pernicious anaemia.[1] In the following year E. L. Rickes and his co-workers[2] in America and Lester Smith[3] in England independently announced the isolation of the anti-pernicious anaemia factor in pure crystalline form from liver concentrates. Particular credit was due to Lester Smith because he was unaware of the microbiological studies of Shorb, and all his liver preparations had to be assayed clinically. He was fortunate in having the assistance of C. C. Ungley, of Newcastle, in this work. The newly isolated principle was called vitamin B_{12} and later cyanocobalamine because it was found to contain cyanogen and cobalt. Cobalt had never been discovered in a naturally occurring substance before, and cyanogen was known to occur only in certain plant glycosides. It was not long before haematologists in collaboration with biochemists showed that vitamin B_{12} was identical with the extrinsic factor of Castle.

The work of the organic chemist, however, did not proceed so smoothly. Considerable effort on both sides of the Atlantic was put into analytical studies aimed at elucidating the structure of the vitamin. In 1949, shortly after its isolation, it was shown that on acid hydrolysis it yielded a 5 : 6 dimethylbenziminazole residue, a cobalt-containing acid, phosphoric acid, ribose, and 1-aminopropanol.[4,5] After this progress was slow. However, the patient work of chemists in the last five years has now borne fruit. At the Annual Meeting of the Chemical Society at Exeter in July, Sir Alexander Todd and A. W. Johnson, of Cambridge, described analytical work which, coupled with *x*-ray crystallography studies



(I) (II) (III)

made by Mrs. D. M. Hodgkin at Oxford, and described by her at the Third International Congress of Biochemistry in Brussels in August, has given the clue to the broad chemical structure of the vitamin B_{12} molecule. These workers have now reported their studies in greater detail.[6,7] In Sir Alexander Todd's laboratory it was shown that the cobalt-containing hydrolysis product yielded on further alkaline hydrolysis a hexacarboxylic acid. This was submitted to Dr. Hodgkin for *x*-ray crystallographic analysis. From a series of calculations the ring system (I) was deduced, in which four five-membered rings are connected through three linking

[1] Shorb, M. S., *J. Bact.*, 1947, **53**, 669; *J. biol. Chem.*, 1947, **169**, 455.
[2] Rickes, E. L., Brink, N. G., Koniuszy, F. R., Wood, T. R., and Folkers, K., *Science*, 1948, **107**, 396.
[3] Smith, E. L., *Nature, Lond.*, 1948, **161**, 638.
[4] Holliday, E. R., and Petrow, V., *J. Pharm. Pharmacol.*, 1949, **1**, 734.
[5] Beaven, G. R., Holliday, E. R., Johnson, E. A., Ellis, B., and Petrow, V., ibid., 1950, **2**, 944.
[6] Hodgkin D. C., Pickworth, J., Robertson, J. H., Trueblood, K. N., Prosen, R. J., and White, J. G., *Nature (Lond.)*, 1955, **176**, 325.
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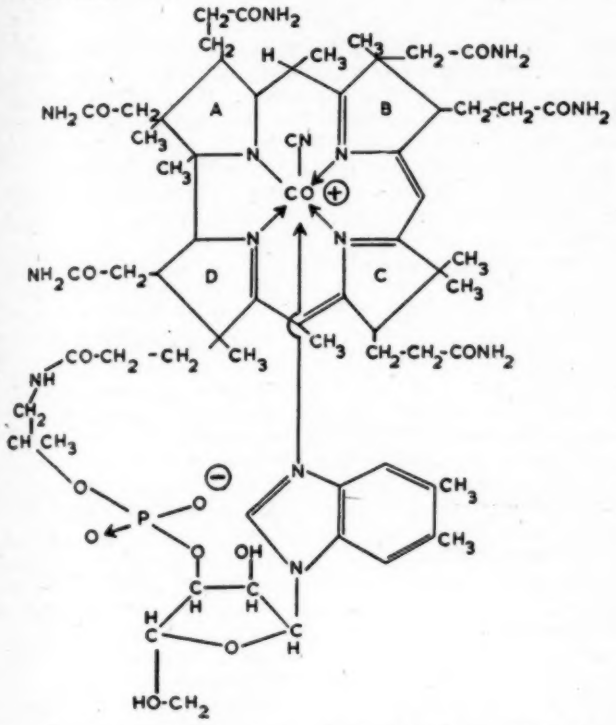
atoms. Workers in the Merck Laboratories in the U.S.A. had meanwhile isolated the two degradation products (II) and (III). *X*-ray crystallographic studies were made on these. Piecing together all the analytical data from the various laboratories, Sir Alexander Todd considers that vitamin B_{12} is a nucleotide of the following structure:



The basic ring structure of vitamin B_{12}, which contains four pyrrole rings, resembles that of haemoglobin and the porphyrins. Even if such a complex structure could be synthesized, it would still be cheaper to make vitamin B_{12} from the culture fluid of *Streptomyces griseus*, its present source of supply. It is made as a by-product in the manufacture of streptomycin.

OCCUPATIONAL DISEASES

Two years ago the Minister of Pensions and National Insurance appointed a committee to review the present provisions of the National Insurance (Industrial Injuries) Act under which benefit is paid for diseases and injuries not caused by accident. Its report[1] now published is signed by nine of the members, including the three medical members[2]; three trade union members dissent from it and have written a minority report. This is a somewhat unfortunate outcome, for the committee was set up in response to what *The Times*[3] has called "trade union pressure," and the three trade unionists begin their minority report by asserting that there is a "growing dissatisfaction among workpeople" with the present limits of the scheme. On one point both groups in the committee are agreed—namely, that more research into occupational health hazards is needed. It is indeed a prerequisite if their opposing views are to be reconciled, for the two groups differ chiefly on the best way to act in our present ignorance of the effect of many occupations on health. The research units run by the Medical Research Council and various universities to investigate occupational and environmental medicine have an important part to play here in elucidating the aetiology of occupational disease.

The chief difference of opinion in the committee arose over the size of the industrial insurance umbrella, and, in effect, whether it should be large enough to cover diseases which are found to be prevalent among people engaged in a certain occupation but are not known to have a specific cause in the occupational environment. Among the conditions which determine whether the Ministry may prescribe a disease as one which entitles its victims to benefit from industrial insurance is that "the attribution of particular cases to the nature of the employment" must be "established or presumed with reasonable certainty." The trade union members contended that the insurance cover is inadequate "for diseases common among the general public which may also be due to special occupational risk." In particular, they thought chronic bronchitis and rheumatic diseases should be eligible for prescription. Aware of the difficulty of deciding in a particular case whether such a disease is to be attributed to the person's occupation or to childhood illness, for instance, or to home environment, these members take what might be called the epidemiological approach. They conclude that "a disease should be prescribable if it can be presumed with reasonable certainty, regardless of individual attribution, that most of the cases in the field covered are occupational."

The administrative difficulties that must be created by the enormous number of claims to be expected under such a scheme evidently alarmed the majority of the committee; moreover, these members were alive to the medical objections to it also. While "it would be futile to expect individual doctors to provide satisfactory answers to questions which the medical profession as a whole could not answer," yet "doctors might feel constrained to try and answer them." "This could lead to a progressive debasing of the currency of medical certification . . . 'bad' certificates tending to drive out 'good.'" Again it is not easy to see the basis on which anyone could decide whether a disease is sufficiently prevalent to constitute an occupational hazard. Coronary thrombosis, for instance, is probably an occupational hazard of doctors, and especially of general practitioners[4]; hypertension is commonly believed to be exceptionally frequent among business executives, duodenal ulcer among salesmen, and cirrhosis of the liver among brewers' draymen. The thorough collection and analysis of morbidity statistics would probably show a surprising number of discrepancies between disease rates in different occupations, if mortality statistics are any guide. At bottom the committee were divided over the question, What is the function of national industrial insurance? But it is not one that came within their terms of reference.

[1] *Report of the Departmental Committee Appointed to Review the Disease Provisions of the National Insurance (Industrial Injuries) Act*, 1955 (H.M.S.O., 1s. 3d.).
[2] Sir Ernest Rock Carling, Dr. L. G. Norman, Dr. Alice M. Stewart.
[3] *The Times*, August 26, 1955.
[4] Morris, J. N., Heady, J. A., and Barley, R. G., *British Medical Journal*, 1952, 1, 503.

EMERGENCIES IN GENERAL PRACTICE

SUDDEN GIDDINESS

BY

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Perhaps the value of unhurried history-taking is nowhere better exemplified than in the case of the patient who complains of sudden giddiness. In most cases a proper analysis and interpretation of the complaint can be achieved by taking a careful history and performing a clinical examination. Ancillary methods of inquiry complete the clinical evaluation but are not essential.

Needless to say, the first requirement is to listen carefully to what the patient has to say about his symptom. Is it giddiness? Or is it something else? The patient who has experienced sudden giddiness usually has little difficulty in conveying to his doctor the fact that there has been some upset of equilibrium. The difficulty is not that giddiness goes unrecognized by doctor or patient, though this may happen, but that some other sensation is misleadingly described or interpreted as giddiness. So terminology becomes important—patient and doctor must know in what sense they use certain words. And perhaps no word is more misused than "giddiness."

Nature of Giddiness

Giddiness is a sensation of disturbed equilibrium. It is not just "faintness," "queer feelings," "muzzy feeling," "light-headedness," "floating," "sick feeling," or any of the many unpleasant sensations that some people experience under certain circumstances, such as on heights or in busy city streets. The person who experiences giddiness nearly always experiences a sensation of movement. His senses are deceived into seeing or feeling movement of one sort or another. His accustomed sense of correct orientation within his environment is temporarily disturbed. This abnormal sensation of movement is not necessarily one of rotation (vertigo). Vertigo is, of course, one of the commonest forms of giddiness; there is a sensation of turning (*vertere*, to turn), either in self, of self, or of the environment. Thus the patient may feel a swirling sensation in his head; he may feel that his whole body is spinning; he may see or feel his surroundings are turning about him. Vertigo is often used in this strict sense—to denote that the sensation of movement is one of rotation. But there is nothing to be gained by adhering to this definition, for we know that other equally distressing forms of giddiness, of identical aetiology and significance, may be characterized not by a revolving sensation but by a sense of falling through space, or by some movement of self or surroundings in any other plane. For example, the patient may describe how the ground rocks beneath him or appears to rush up towards him. He may see walls or objects tilting this way or that; the ceiling may look as if it is falling in or the pavement as if it were swaying. Or, bewildered, the patient may only be able to exclaim, "Nothing will stay still."

A given patient in different attacks of giddiness usually has much the same experience; the pattern of his vertigo remains the same, varying only in intensity and duration. Less often the actual illusions of movement vary in different episodes. Occasionally patients with paroxysmal vertigo and its characteristic accompaniments do not seem to experience a sense of movement of any sort. They may stagger, fall, and vomit, but afterwards deny that their giddiness consisted in any abnormal sensation of movement.

Whatever form the giddiness actually takes the patient will try to clutch hold of something or sit or lie down. He may close his eyes in an attempt to shut off the distressing impressions of movement. Pallor, sweating, nausea and vomiting, even diarrhoea, may follow. The patient not only feels very ill and prostrated but his appearance may be alarming. The total picture may suggest some catastrophic illness or food-poisoning, not a transient upset in one ear. If the vertigo is abrupt and severe the patient will fall to the ground, perhaps staggering about in a drunken manner at first. He may injure himself trying to get upstairs to bed; he may be concussed. Occasionally he may go down like a log, without warning, but later he may recollect feeling a sensation of movement as he fell. At other times he seems just to "fold-up" as if all sense of posture had left him; he drops to his knees in an inexplicable fashion.

Sudden attacks of vertigo are usually spontaneous and irregular in occurrence; they may appear at any time of the day or night, when awake or when sleeping. In one variety the attacks are provoked by certain movements or the adoption of a certain posture. Turning the head or body, changing from the horizontal to the upright position, lying on one side, bending down, or looking upwards are examples of such movements. Consciousness is rarely affected. Between attacks the patient may feel perfectly well in respect of his sense of balance, but some patients may feel a more or less continuous state of unbalance. Rarely the doctor is consulted before any acute episode is experienced. The vagueness of the sensations may suggest a diagnosis of neurosis. Vertigo may therefore present as paroxysmal vertigo, postural or positional vertigo, or as chronic vertigo.

Aetiology

Correct orientation of the body requires information provided by the retinae, the proprioceptors of the muscles of the eyeballs, neck, trunk, and limbs, and above all by the two labyrinths. The co-ordination of the afferent impulses derived from these sources is effected by the vestibular nuclei and the posterior longitudinal bundle in the brain stem, by the cerebellum, and by the temporal lobes. Vertigo may therefore result from a lesion of the sensory end-organs, of the afferent paths, or of the central mechanisms. In practice nearly 90% of cases of vertigo are due to labyrinthine lesions.

Causes of Giddiness

Peripheral Lesions:

1. Aural:—Ménière's disease; vestibular neuronitis; positional vertigo; trauma; infection (mumps, measles, herpes zoster, meningitis).
2. Ocular:—Diplopia.

Central Lesions:

1. Acoustic neuroma.
2. Brain stem:—Disseminated sclerosis; thrombosis of the posterior inferior cerebellar artery; tumours.
3. Cerebellum:—Tumour; haemorrhage and thrombosis.
4. Cerebral:— Raised intracranial pressure; tumours; arteriosclerosis; epilepsy; migraine; drugs (barbiturates, phenytoin sodium, streptomycin, etc.).

Preliminary Investigation of the Patient

During an attack of acute vertigo a brief examination is usually possible.

Aural.—Is there any gross impairment of hearing? The external auditory meatus should be examined for wax, evidence of otitis media, or herpes zoster.

Nystagmus.—During an attack of aural vertigo the patient usually lies on the sound side. If he opens his eyes and looks

upwards to the affected ear, nystagmus will be seen. If he is lying on his back, the nystagmus is increased in amplitude when the eyes are turned to the sound side.

Ocular Movements.—Severe vertigo rarely results from diplopia. In most instances of diplopia there is no falling or sickness.

Ocular Fundi.—Raised intracranial pressure may itself cause some vertigo, and posterior fossa tumours will also cause ataxia and vomiting. Swelling of the optic disks and vascular engorgement may already be present.

On recovery a more careful examination can be made.

Aural.—Is there impairment of hearing on either side? Is the deafness conduction (middle ear) or perceptive (nerve) in character? These may be distinguished by the standard tuning-fork tests. *Weber's Test:* When a vibrating tuning-fork is placed on the vertex of the skull, the sound is best heard in the deaf ear in conduction deafness, and in the good ear in perceptive deafness. *Rinne's Test:* Normally air conduction is better than bone conduction, so that a vibrating tuning-fork is better heard when held near the ear than when its base is placed on the mastoid process (the ear being closed by the observer's finger). In conduction deafness the sound cannot be heard by air conduction after bone conduction has ceased to transmit it; in perceptive deafness the reverse is true. Special tests are necessary to distinguish the two forms of perceptive deafness—namely, lesions of the cochlea and lesions of the auditory nerve. Auditory function and vestibular function may be further investigated in hospital.

Ménière's Disease (Recurrent Aural Vertigo: Endolymphatic Hydrops)

Successive attacks of swelling of the membranous labyrinth with eventual irreversible changes are responsible for the well-known sequence of clinical events. Attacks of vertigo, vomiting, and prostration are usually associated with tinnitus and increasing deafness. The vertigo usually lasts several hours at a time, rarely more, and may take any of the forms described above. It is a disorder of middle life and is slightly more common in males; most patients have their first attack before the age of 50. The disease usually affects one labyrinth before the other and appears to involve both cochlear and vestibular components from the start. There is considerable variation in the order of appearance of the three symptoms—vertigo, deafness, and tinnitus. Most commonly vertigo and deafness are first noticed at about the same time. The disease runs a protracted course with phases of activity and quiescence. Thus attacks may appear in groups; for several weeks at a time tinnitus may be loud and persistent, and the hearing distorted or impaired. The patient may feel that one or both ears are "blocked" or "full" and that his sense of balance is "not just right." There may be complaint of headache or "fullness" or "pressure" about the head, and sedentary workers may find concentration difficult. It is during such active phases of the disease that sudden vertigo is especially apt to occur, and the experienced sufferer, by noting such symptoms, may be forewarned of the acute attack.

There is nystagmus with the quick component toward the affected ear, which, as the patient lies on his side, is usually uppermost. The nystagmus subsides with the vertigo and is not usually to be found during intervals of complete freedom. Deafness, on the other hand, tends to be progressive and is of perceptive type. Each attack or group of attacks tends to leave some further impairment of hearing. The classical tuning-fork tests reveal that bone conduction of sound is reduced as well as air conduction.

Vestibular Neuronitis and Paroxysmal Positional Vertigo

The term "vestibular neuronitis" has been applied to a group of cases in which vertigo due to vestibular disturbance is unassociated with any cochlear involvement. There is no tinnitus or deafness but caloric responses are reduced. The affection is seen in a younger age group (30 to 50 years), the vertigo is less paroxysmal, and there may be only one attack. The pathology is not known but it is thought to be in the nature of a selective lesion of the vestibular nerves or nuclei. It may follow respiratory infection or appear to be associated with focal sepsis; it may account for some forms of so-called "epidemic vertigo."

In paroxysmal positional vertigo there is usually not only no involvement of the cochlear apparatus but caloric tests are normal. Nystagmus and vertigo are provoked by certain movements or critical positions of the head. It appears to arise from a non-progressive lesion of the otolith apparatus or from one more centrally placed in the vestibular pathways. The nystagmus and vertigo can nearly always be made to "fatigue" by repetition of the particular movement which provokes them in the first place.

Both vestibular neuronitis and positional vertigo are less incapacitating than Ménière's disease and run a milder course, usually terminating spontaneously. Their separation from the condition of endolymphatic hydrops renders further use of the term Ménière's syndrome inappropriate. What Ménière described was a disease *sui generis* of the internal ear.

Injury and Infection of the Labyrinth

Vertigo and distortion or impairment of hearing, or both, may follow a head injury, especially when there has been a fracture through one petrous temporal bone. If impairment of hearing does not draw attention to the internal ear the true nature of the symptoms may not be appreciated. Caloric tests are helpful.

Chronic middle-ear infection sometimes leads to involvement of the bony labyrinth. Vertigo may be acute or chronic and may be aggravated by any increase of pressure in the middle ear. The general health of the patient often deteriorates and aural surgery is necessary. Involvement of the labyrinth may occur during the course of certain acute infections such as mumps, measles, or meningitis. In the Ramsay Hunt syndrome (facial palsy and otitic herpes) vertigo is often a feature.

Posterior Fossa Tumours

In general, tumours in this region present with symptoms of intracranial hypertension or disturbance of balance, or both together. The commonest tumour in this situation is an acoustic neuroma growing in the cerebellopontine angle. Vertigo is a common symptom and it is often paroxysmal as in Ménière's disease. In both conditions tinnitus and nerve deafness are usually present, though not necessarily complained of or related to the vertigo. In the tumour case the complaint of giddiness is probably commoner than the complaint of deafness, while symptoms of intracranial hypertension or of involvement of adjacent cranial nerves may be absent. Differential diagnosis may therefore be difficult. With acoustic neuroma there is often a story of numbness or stiffness on one side of the face and the corneal reflex may be absent. Disturbance of gait tends to be progressive and independent of vertiginous episodes. The tumour patient may recognize that this loss of balance is due to lack of control over his limbs and not to some disturbance in his head. This should be put to him. He may also have noticed that one upper limb is clumsy when there is no question of disturbed balance—as when he is sitting down or reclining. The nystagmus in the tumour case is not restricted to periods of vertigo and its fast-component is to the opposite side.

Brain-Stem Lesions

Sudden involvement of the vestibular connexions in the brain stem, as in disseminated sclerosis or thrombosis of the posterior inferior cerebellar artery, provokes vertigo. In disseminated sclerosis there is no evidence of cochlear disease and the vertigo and nystagmus are usually, but not always, accompanied by signs of involvement of other nuclei and tracts. There may be diplopia and sensory symptoms. Recovery is less prompt than in aural vertigo. Thrombosis of the posterior inferior cerebellar artery may lead to ptosis with impairment of pain and temperature sensation on the same side of the face and on the opposite side of the body.

These signs may be noticed by the patient when he shaves or takes a bath.

Tumours of the brain stem are more likely to give rise to a sensation of chronic giddiness with nystagmus. Localizing signs are seldom late in making their appearance.

Management

The management of an acute attack of giddiness is the same whatever its cause. The following description, however, is related to Ménière's disease, as this is by far the commonest cause.

The patient should not be moved unnecessarily during the height of the acute attack. He should be allowed to lie down in a comfortable position of his own choosing as soon as possible. Many patients will later describe that the journey upstairs, dragged there by misguided members of the family, the undressing, and the getting into bed were the worst experience during the illness.

As soon as possible patient and family must be reassured. The episode is alarming, but it will subside in a few hours and the illness is never fatal or paralysing. No drug has a specific effect on vertigo, but phenobarbitone has a general sedative effect and perhaps reduces the sensitivity of the labyrinths. An intramuscular injection of sodium phenobarbitone, 3 gr. (0.2 g.), should be given immediately and oral phenobarbitone, ½ gr. (32 mg.), three times a day, should be continued for some weeks afterwards and during the phases when the patient feels that attacks are "just around the corner." In Ménière's disease seasickness remedies such as hyoscine and antihistamines—for example, promethazine and dimenhydrinate—may be helpful but are in no way specific. Fluids should not be pushed in an effort to correct acidosis or dehydration consequent on vomiting, as this may precipitate further attacks. Fluids should be restricted for a week or two to 2 pints (1.1 litres) in twenty-four hours and salt should be omitted from cooking and at table. There is no certain evidence that this "antiretentional" regime needs to be continued indefinitely. The patient should be advised to adopt it when he suspects a repetition of the attack.

In Ménière's disease the use of vasodilator drugs such as histamine and nicotinic acid and the search for focal sepsis or allergens all have their advocates, but in my experience are not rewarding. The course of the disease is extremely variable and most patients who have been reassured manage reasonably well by restricting their activities, using phenobarbitone, learning to recognize premonitory symptoms, and going to bed. The unexciting nature of such advice may be unacceptable to some patients or their doctors, but in the present state of knowledge it applies to the majority of patients with Ménière's disease. When periods of remission do not occur and attacks cannot be modified by such measures the question of destruction of one labyrinth by alcohol injection, diathermy, or removal of the external semicircular canal will have to be considered. Section of part or whole of one auditory nerve is a serious intracranial operation which has little part in the treatment of this disease.

When the acute attack of vertigo has subsided a general overhaul, with aural and neurological examination, is advisable. Lesions outside the ear and nervous system seldom produce paroxysmal vertigo.

Next article on Emergencies in General Practice.—"Diphtheria," by Dr. A. B. Christie.

Refresher Course Book.—Copies of the second volume of collected articles from the Refresher Course for General Practitioners are still available at 25s. (postage 1s.) each from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller. The first volume is now sold out.

BIOCHEMISTRY AND CLINICAL MEDICINE

CONTRIBUTIONS FROM THE THIRD INTERNATIONAL CONGRESS, AUGUST, 1955

[FROM A SPECIAL CORRESPONDENT]

The Third International Congress of Biochemistry, held at Brussels from August 1 to 7, was attended by over 2,000 delegates from all parts of the globe, including a large group from the Soviet Union. Some idea of the scope of modern biochemistry can be gathered from the fact that the congress was subdivided into 17 sections, all of which presented a full programme. As a result it was impossible, as at many such international gatherings, to attend more than a small proportion of the meetings in person. While no world-shaking discovery such as would necessitate a major reorientation of current biological theory was announced at the congress, there were plenty of papers of clinical interest, and it is with some of these that this report is mainly concerned.

Metabolic Disorders

In the section of pathological chemistry and immunology, H. HARRIS (London) opened a discussion on amino-aciduria in man. After explaining that a normal adult excretes about 1.1 g. of amino-acids daily, together with 2 g. in the combined form including peptides, and discussing techniques of estimation, he went on to classify the pathological amino-acidurias. He divided them into "overflow" and "renal." In the former category were liver diseases and phenylketonuria, in the second group cystinuria, Wilson's disease, galactosaemia, the Fanconi and similar syndromes, scurvy, rickets, and lead and lysol poisoning. The speaker made it clear that, despite many uncertainties, the main factor in the first category is a raised blood level of amino-acids, and in the second category defects of tubular reabsorption. In another paper, B. H. BILLING and G. H. LATHE (London) summarized their work on jaundiced serum. They have identified three bile pigments in such sera; a fat-soluble one, giving the "indirect" van den Bergh reaction and identified as bilirubin, and two water-soluble pigments giving the "direct" van den Bergh reaction. During the excretion of bilirubin in the bile the pigment is converted to one of these two water-soluble pigments.

A contribution to the curious metabolic disorder of children known as gargoylism was made by L. L. UZMAN (Washington, D.C.). He had isolated from the spleen the storage substance that accumulates in the cells of these patients and fractionated it. The material comprised two components; fraction S consisting of fatty acids, hexoses, hexosamine, hexuronic acid, and neuraminic acid; and fraction P, a sulphate ester polysaccharide of high molecular weight whose sugars are glucose and galactose and which also contains glucosamine and hexuronic acids. Another communication of paediatric interest was given by M. REINER, D. H. HIGGINBOTHAM, and A. PATZ (Washington, D.C.). They had investigated in animals the mode of action of high oxygen levels in causing retrolental fibroplasia in immature retinae. At concentrations of 50% and above oxygen caused vasoconstriction of the retinal vessels. Total obliteration was found at concentrations of 80–100%. But the vasoconstriction was not irreversible until after three days of continuous exposure to high oxygen levels; it was not reversed by adding 5% carbon dioxide to the oxygen.

Protein Chemistry and Hormone Structure

The section of protein chemistry revealed steady progress in many fields. P. H. BELL and R. G. SHEPERD (Stamford, Conn.) described their work that had led to the purification and structural analysis of β-corticotrophin (A.C.T.H.) and issued the audience with charts showing the complete amino-acid sequence of the molecule of this hormone. C. H. LI (Berkeley, Calif.) produced further evidence showing that the

biological activity of growth hormone is not dependent upon the integrity of the protein but resides in only a part of the molecule. J. HOREJSI and R. SMETANA (Prague) reported a new method for the separation of gamma globulin from blood plasma using 2-ethoxy-6,9-diaminoacridine. V. A. BELICER (Kiev) discussed his work on protein denaturation. He interpreted his results as showing that the initial step in the process is rupture of the weak bonds in the amino-acid side chains. B. G. BENFEY (Montreal) and J. L. PURVIS (Quebec) have isolated an apparently pure melanophore-expanding hormone from hog pituitary, while S. SHULMAN and E. WITEBSKY (Buffalo, N.Y.) reported the isolation of five different proteins from hog thyroid, some of which have been prepared in a high state of purity.

In the field of nucleoprotein chemistry, advances were mainly in the direction of structural analysis of the molecular components. Thus P. W. KENT, P. F. V. WARD, and C. S. ENNIS (Oxford) have used replacement and degradation techniques to investigate the sequence of pyrimidine nucleotides in desoxyribonucleic acids. E. POLLI and G. SEMANZA (Milan) reported physico-chemical differences between the desoxyribonucleic acids of normal and leukaemic leucocytes.

H. BORSOOK (Pasadena, Calif.) contributed a masterly report on the present state of knowledge regarding the biosynthesis of body proteins. He described the two main hypotheses that exist: the "templet" theory in which amino-acids are believed to join and leave a relatively intact protein molecule; and the other hypothesis which postulates that the protein molecule is built up from amino-acids by way of peptides. He thought the "templet" theory was the correct one. In the lively discussion that followed, opinion was clearly in agreement with this view. T. WORK (London), however, although not strongly challenging the "templet" hypothesis, was able to report that he and his colleagues have isolated a large number of hitherto unsuspected peptides from liver. The question is, if peptides play no part in protein synthesis, why are they demonstrable in protein-forming tissues?

Metabolism of Normal and Malignant Cells

In the section of cellular biochemistry, A. E. MIRSKY (New York) gave a general talk on the relation of the biochemistry of the cell nucleus to the nature and activity of the chromosomal and hereditary material. It was interesting to observe how the study of the cell nucleus and its chemical constituents is coming to predominate over interest in the cytoplasmic counterparts. Nevertheless nuclear biochemistry is in its infancy, and Mirsky's lecture was to a large extent devoted to a discussion of the nucleoprotein molecule.

In the field of neoplasia, H. J. CRUFT, C. M. MAURITZEN, and E. STEDMAN (Edinburgh) reported physico-chemical differences between the histones (simple proteins of basic character) of the nuclei of malignant and normal cells. L. G. H. LEDOUX (Brussels), contributing to a subject that has excited some interest because of its possible therapeutic implications, described the regression of ascites tumour after the administration of ribonuclease, an enzyme that hydrolyses ribonucleic acid. The action of this enzyme on the tumour cells *in vitro* appears to be complex.

D. P. GROTH (Brussels) reported that crystalline ribonuclease inhibits bacterial growth and the incorporation of glycine into the bacterial protein, but not into the nucleic acid purines.

B. E. HOLMES and L. K. MEE (Cambridge) gave a preliminary report on the uptake of labelled formate by the desoxyribonucleic acid of liver nuclei during regeneration in the mitotic and pre-mitotic phases. F. GROS-DOULCET, F. GROS, and S. SPIEGELMAN (Illinois) reported on an investigation into whether protein and ribonucleic acid synthesis are dependent on desoxyribonucleic acid (D.N.A.) turnover. Using bacteria, they obtained protein synthesis in the absence of D.N.A. formation. These observations are of importance in relation to the unsolved problem of the dependence or otherwise of protein synthesis in cells, and therefore of growth, on the self-reproduction of D.N.A. molecules. More data on the growth-inhibiting powers of ribonuclease was presented by J. LECLERC (Brussels), who described the cessation of the multiplication of influenza virus in the presence of ribonuclease. J. BRACHET (Belgium) reported similar effects of the enzyme on cancer cells, amoebae, and ova, stressing its penetration into the cells.

D. A. SALZBERG (Palo Alto, Calif.), investigating the mechanism of azo-dye carcinogenesis, found azo dyes to be capable of replacing riboflavine as a growth factor for certain micro-organisms of the *Neurospora* group. It was interesting to observe how widely nowadays suitable strains of micro-organisms are being used to investigate growth phenomena in mammalian cells.

Hormone Assays and Other Biochemical Tests

In the section of clinical chemistry much attention was directed to the steroid hormones. J. K. NORYMBERSKI and R. D. STUBBS (Sheffield) described a new method, using zinc dust in 50% acetic acid, for the differential analysis of urinary 17-ketogenic steroids. J. R. HODGES (London) reported a new method for the bioassay of corticotrophin which obviated the need for hypophysectomy in the rats used, endogenous corticotrophin activity being suppressed by preliminary dosage with deoxycortone. J. W. H. LUGG and J. M. BOWNESS (Singapore) communicated results indicating significant differences in the total daily output of urinary 17-ketosteroids in different ethnic groups, but not in the relative proportions of the steroids. R. D. BULBROOK, F. C. GREENWOOD, and J. STRETTON-YOUNG (London) reported a correlation between the cytology of vaginal mucosa, using vaginal smears, and the amount of oestrone or oestriol, but not oestradiol, in the urine. Despite this they could not obtain an unequivocal estimate of endogenous oestrogen production in any given case.

P. L. MUNSTON, G. W. THORN, J. H. HARRISON, and M. C. SHEPS (Boston) reported an improved method for the bioassay of urinary androgens. With its aid they were able to show that elderly men with prostatic carcinoma excreted no more androgens than normal controls of the same age. They also found that androgen excretion fell shortly after orchidectomy, showing that the testis was still producing androgens despite the patient's age and condition. Adrenalectomy produced a further decrease in excretion, and corticotrophin increased it whether the testes were present or not. As a result of metabolic studies they concluded that the adrenal cortex produces androgen precursors other than the glucocorticoids. M. QUINTILIANI and R. ANGELICO (Rome) gave a preliminary communication of the technique of obtaining corticosteroid synthesis *in vitro* from the adrenal glands of rats.

In other fields of interest to clinical chemists, an improved method for the separation of different haemoglobins by paper electrophoresis was reported by C. A. J. GOLDBERG (Philadelphia). The method involves the addition of glycerol to the normal buffer commonly used. O. BASSIR (Beverley) reported on molecular inhomogeneity of inulin as a source of error in inulin-clearance tests. A. J. ANDERSON, E. LOCKEY, and N. F. MACLAGAN (London) described their work on urinary and serum levels of mucoproteins in health and various disease states. Raised values were found in cases of cancer, especially if lymph nodes were involved.

Human Nutrition

I. MACINTYRE, J. E. S. BRADLEY, and D. DAVIDSSON (London) reported their new method for estimating total body water and extracellular fluid using tritium and radioactive bromide respectively and improved counting techniques. By using radioactive krypton they were able to estimate total body fat by calculation from the distribution of this inert gas.

In the section of nutrition J. H. VAN DE KAMER and H. A. WEIJERS (Utrecht) reported that the harmful influence of wheat in coeliac disease is probably due to glutamine.

although only as a constituent of gliadin, the wheat protein. They found that blood glutamine levels rose in coeliac patients after oral dosage with gliadin. A. C. FRAZER, C. A. C. ROSS, and H. G. SAMMONS (Birmingham) also reported the toxicity of gliadin in coeliac disease. Several communications on Castle's intrinsic factor were read. A. L. LATNER, R. J. MERRILLS, and L. RAINE (Newcastle) reported the preparation of intrinsic factor in a highly purified state, apparently homogeneous on electrophoresis, ultracentrifugation, and chromatography. Intrinsic factor is a mucoprotein with a molecular weight of between 10,000 and 20,000.

A. BONDI and Y. BIRK (Israel) found plant protein to yield large peptides resistant to the action of proteolytic enzymes. Animal protein did not contain such peptides and their results suggested to them a possible reason for the superior quality of animal protein in nutrition.

The section of chemical pharmacology produced a large variety of communications on numerous topics. C. H. GALLAGHER, J. D. JUDAH, and K. R. REES (London) had investigated the mode of action of thioacetamide, a compound causing liver necrosis and regeneration, possibly carcinomatous. The hepatic necrosis was associated with a great increase in the amount of calcium in the liver cells, which might inhibit intracellular enzyme activity. Antihistamine drugs prevented the toxic effect of thioacetamide, and this and the calcium accumulation suggested to the authors a possible permeability effect.

Conclusion

It is difficult to sum up a scientific meeting covering as many topics as the Third International Congress of Biochemistry. One thing that did emerge, however, was the great amount of work now being devoted to the nucleoproteins and the prominence being given to such studies by those concerned with the cancer problem. Another feature of the congress was the steady progress apparent in the analysis of the chemical structure of proteins. Both this field and that of the chemistry of the cell nucleus reflect a trend towards precision of description and analysis and a tendency not to be contented with vague details of the structure of chemical compounds of biochemical interest. It is almost as if biochemistry were becoming more chemical and less biological.

In one respect the congress was disappointing. This was its failure to introduce any wholly new work on the achievement of respiratory enzymic activity and energy transformations in soluble as opposed to particulate systems. It seems reasonable to predict that by the time the Fourth International Congress is held in Vienna work of this nature will occupy a prominent place and will have led to notable advances.

APPROVED NAMES

Approved Names are devised or selected by the British Pharmacopoeia Commission, and the intention is that if any of the drugs to which these Approved Names are applied should eventually be described in the *British Pharmacopoeia*, the Approved Name should be its official title. The last list of approved names was published in the *Journal* of June 18, 1955 (p. 1473).

Approved Name	*Other Names*
Aldosterone	11β : 21 - Dihydroxy - 3:20-dioxo-4-pregnen-18-al. "Electrocortin"; "aldocorten."
Amiphenazole	2 : 4 - Diamino - 5 - phenylthiazole. "Daptazole."
Bemegride	β-Ethyl-β-methylglutarimide. "Megimide."
Demecolcine	Deacetylmethylcolchicine. "Colcemid."
Glutethimide	α-Ethyl-α-phenylglutarimide. "Doriden."
Normethadone	6-Dimethylamino-4:4-diphenylhexan 3-one.
Oxycinchophen	3-Hydroxy-2-phenylcinchonic acid.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Treatment of Barbiturate Poisoning

SIR,—Dr. A. Shulman's letter (*Journal*, July 30, p. 322) commenting on our paper (*Journal*, April 23, p. 1022) raises many interesting points.

Gastric Lavage.—There are clearly two possibilities to consider: the drug is either in the stomach (or the oesophagus) or it has passed through the pylorus. It is obviously futile to expect to recover by lavage that portion which has left the stomach. We do suggest, however, that it is always reasonable to perform gastric lavage in the hope of recovering some of the drug which *may* still be in the stomach. We should like to ask Dr. Shulman what he would do if a man said to him: "Doctor, ten minutes ago I swallowed 100 phenobarbitone tablets." It may be objected that the interval between taking the drug and starting treatment is rarely a matter of minutes but a few hours. At the time of the emergency, however, it is notoriously difficult to get reliable information on this point, and not infrequently the stated duration of narcosis is little more than an intelligent guess. Nor is time the only factor: the narcosis may be due to the immediate effects of sodium amytal, but who can say that there are not also a hundred tablets of phenobarbitone—the action of which has scarcely begun? Again, even when a long interval has elapsed before the start of treatment, it is by no means certain that barbiturate tablets or particles will not be present in the stomach or the oesophagus. In a case seen by one of us (S. A.) in a hospital abroad, tablets were recovered from the lower end of the oesophagus at post-mortem examination: for reasons which seemed excellent to the receiving physician, gastric lavage had not been carried out.

If, in fact, there is no barbiturate in the stomach, gastric lavage is valueless—but, if properly conducted, it is also harmless. Perhaps Dr. Shulman will reply that he does not deny the importance of emptying the stomach but that he prefers aspiration. We cannot agree that aspiration is the treatment of choice in the early stage of barbiturate poisoning; and in the later stages, if lavage is useless so also is aspiration. Dr. Shulman warns us against the danger of expediting the absorption of barbiturate by using large quantities of fluid during lavage. We emphasized the same point: "Not more than half a pint (300 ml.) should be poured into the funnel at a time, because large volumes of fluid entering the stomach tend to drive the gastric contents through the pylorus." In support of his criticism of gastric lavage Dr. Shulman quotes Scandinavian workers who treated 100 serious cases of barbiturate poisoning by this method and found negligible quantities of the drug in the stomach washings. But these observations merely prove that gastric lavage was started too late—when nearly all the drug had passed through the pylorus; they do not invalidate the proposition that poisons lying in the stomach should be removed. That this is the correct interpretation is supported by the fact that the cases were all regarded as "serious" when first seen—meaning, we suppose, that there was deep coma consistent with complete, or almost complete, absorption of the drug.

We would repeat, therefore, that competent gastric lavage should not be omitted: inevitably it will often be useless, but it should never be harmful, and occasionally it will be life-saving.

Sodium Bicarbonate.—Is often recommended for gastric lavage because it facilitates the removal of viscid mucus. We think it unwise, however, to use sodium bicarbonate in barbiturate poisoning, because insoluble preparations are likely to be converted to the soluble sodium salts and this hastens their absorption. Dr. Shulman's comments refer to the effects of sodium bicarbonate after absorption—an entirely different matter. We agree that if a mild alkalosis favours renal excretion of barbiturates administration of sodium bicarbonate may be justified. Two points, however, should be noted: (1) For the reasons stated above and because of the abnormal state of the alimentary canal in a deeply comatose patient, the sodium bicarbonate should not be given by mouth but by intravenous infusion. (2) In the later stages of coma, intravenous infusion of sodium bicarbonate solution would help to rectify the inevitable starvation ketosis.

Aperients.—Dr. Shulman refers to the possible harmful effects of aperients which would "serve as a source of irritation" in the atonic bowel. Our paper contained no recommendation of irritant purgatives. We mentioned magnesium sulphate. The

function of this salt is to hinder the absorption of water from the lumen of the bowel and thus to delay the transfer of barbiturate to the blood stream. In the conditions under review—where an excess of water is available—magnesium sulphate is not an irritant.

Analeptics.—We welcome Dr. Shulman's authoritative comments on the merits of various analeptics available for the treatment of barbiturate intoxication. We entirely agree that "excessive doses" should not be used. He says that "there is still an inadequate individual index" for detecting such doses of analeptics. It seems to us highly improbable that the situation will ever be otherwise. Separate tests, such as pressure on the supra-orbital nerves and recording the tendon reflexes, are admittedly unreliable. Nevertheless, by taking into account the whole clinical picture, the experienced doctor can nearly always recognize that the patient is regaining consciousness. We reject the suggestion of a fixed dose—implicit in his quoted statement referring to the use of amphetamine by other workers: "The suggested routine under these conditions [respiratory depression] is the intramuscular administration of amphetamine sulphate (25 mg.)." It must be emphasized that the dose of an analeptic is that quantity which produces the desired result. The spacing of the dose fractions is a matter which can be decided only by the physician in charge of the individual patient. We note that it is Dr. Shulman's practice when using 2:4-diamino-5-phenylthiazole hydrochloride ("daptazole") to give parenteral injections of 10 mg. at intervals of five minutes until satisfactory ventilation is obtained. Although, in this department, we are trying to determine the value of the newer analeptics, we are not yet prepared to express a firm preference for these as compared with amphetamine.

Finally, Dr. Shulman refers to the "excellent results" claimed by various authors who use analeptics sparingly but adopt "a thorough routine of medical management." It is well known that when a team of workers in an institution make a comprehensive study of a particular malady the results reflect their enthusiasm and attention to detail. In these circumstances it is not surprising to find that in every aspect of their work the standards are well above the average attained elsewhere. Such developments often provide models of therapeutic efficiency. However, they also create difficulties for an independent observer trying to assess the team's claims regarding the value of a new drug or the effect of withholding a particular therapeutic procedure. It is against this background that we have to examine new methods in the management of barbiturate poisoning. For obvious reasons mortality figures must be scrutinized with special care: their deficiencies can be made good only by resorting to controlled experiments; and designing such experiments within the limits of our code of ethics may well tax our ingenuity to the limit.—We are, etc.,

T. J. THOMSON.
STANLEY ALSTEAD.

Glasgow.

Fluorohydrocortisone and Adrenal Hyperfunction

SIR,—We have read with interest the report by Drs. C. L. Cope and R. J. Harrison (*Journal*, August 20, p. 457) on the effect of 9α-fluorohydrocortisone in a case of Cushing's syndrome. We have carried out suppression tests of this type in four cases of Cushing's syndrome due to adrenal cortical hyperplasia; 10 mg. was given daily in one case for five days and in the others for three days. The effect on the adrenals was assessed by measuring the urinary excretion of 17-ketosteroids, 17-ketogenic steroids, and 17-hydroxycorticoids. In one case all three showed a transient reduction; in one the 17-ketogenic steroids and the 17-hydroxycorticoids fell but the 17-ketosteroids were unchanged, and in the third the 17-ketosteroids and the 17-ketogenic steroids fell but the 17-hydroxycorticoids were not altered. In the fourth case, the most severe if assessed by hormone excretion, there was no definite response, although there was a gradual decline after the 9α-fluorohydrocortisone was stopped. It is of interest that the patient who was given 9α-fluorohydrocortisone for five days showed marked depression of steroid excretion on the first and second days and that after this the output increased.—We are, etc.,

J. D. N. NABARRO.
G. WALKER.

London, W.1.

"Veripaque"

SIR,—Might I make some observations on statements recently published in the *British Journal of Radiology*[1] concerning the above preparation? I had the privilege of carrying out at St. Mark's Hospital for Diseases of the Bowel a series of investigations using "veripaque" in 120 patients at apparently the same time as Drs. J. W. McLaren, King, and Copland were conducting their investigations elsewhere. I feel it would be in the interests of the profession to record our impressions concerning the action and results of this drug, because at St. Mark's we have not received a favourable impression of its action. One of my colleagues observed that the evacuation radiographs (to which Dr. McLaren attaches importance) were quite useless, with the mucosa stripped entirely of barium throughout the whole bowel in 75% or more of the cases.

There is nothing really new about this preparation, which, essentially, is simply a very powerful purgative, somewhat similar in action to, and as powerful as, phenolphthalein. In its original form it came to my notice as far back as 1952 under the name of "neodrast." It next made a reappearance in this country heralded as "colonopaque," and finally we now hear of its rebirth as "veripaque." I have good reason to believe that this drug has been discarded by most American opinions, and also rejected for use in enema work at St. Mark's. The paper published by Drs. McLaren, King, and Copland follows very closely the lines and details of that published by L. B. Schlegel.[2]

The patients examined in my series followed one of three types of investigation: (1) patients treated with premedication by colonic lavage using sodium bicarbonate only in the wash-out solution, and then followed by the opaque enema combined with veripaque; (2) cases of severe constipation without any prior medication and using veripaque in the opaque enema only; (3) cases prepared by colonic lavage with veripaque in the wash-out but no veripaque in the opaque enema. The results were most disappointing, and were certainly not up to the standard of patients prepared by the routine technique of premedication with mild aperients followed by "double-flow" colonic lavage prior to the actual administration of the opaque enema.

Dr. McLaren and his co-workers think they have rediscovered the normal movements of the colon, using veripaque. The colon walls contain a mass of highly sensitive fine nerve termini forming numerous complicated delicate plexi, such as Auerbach's plexi, Meissner's plexi, etc., controlling the action of the longitudinal and circular musculature of the bowel walls. When veripaque is suddenly run into the colon, from the rectum to the caecum, these very sensitive nerve fibrils are violently stimulated by this powerful purgative. In some of my patients the reaction was almost volcanic. They experienced great pain, broke into beads of perspiration; and one said she felt she "would like to die." How could such a violent stimulation be recorded as presenting the movements of a normal bowel? And no wonder the caecum can be seen to assume a violent and unusual contraction and curl up upon itself, being the only unattached and free end of the colon. If a pin is stuck into a worm near one of its ends, it also sharply curls its end upon itself. The movements of a colon violently stimulated by veripaque are far from normal, and indeed rather resemble those of a patient who has had an overdose of strychnine injected. For many years at St. Mark's we in the *x*-ray department have accepted that the primary stimulation in the colon starts by contraction at approximately the recto-pelvic junction. The early-morning cup of tea usually arouses stimulation in this area, gentle at first, then gradually increasing in power of contraction. Soon local gas collection may occur in the rectum and subsequently the desire to defaecate comes on. With the rectum filled, the pressure contraction from the recto-pelvic area empties these sections of the bowel at stool. Should the act of defaecation not be permitted at the moment of call, the contracting mechanism in the recto-pelvic junction eventually relaxes. Some patients can actually feel this relaxation, with the bowel contents regurgitating back into the pelvic section with its highly mobile and astonishing telescopic muscle expanding and making way for the return of faecal material, until another peristaltic wave returns later on. If, however, the call to stool is allowed to function and the act of defaecation carried out, resulting in the emptying of the rectum and sigmoid, then some short time later the faecal collection of the descending section moves down, to be later followed by another *sectional* movement of the transverse section, and subsequently the

contents of the caecum and ascending sections also move on. The movements are sectional and not a general mass movement of the whole bowel, as once believed by some. Veripaque produces general stimulation of the colon which, in my experience, does not represent the normal action of the colon.

Further, if the bowel is stimulated generally and violently it is no longer a normal bowel, and how could any classification of, say, colitis, based upon the appearance of the muscle tone and action, as I outlined briefly in a letter in the *Lancet*,[3] or, indeed, any other classification of colitis, survive ?

At the present time there is no procedure better than that of first softening up the faecal material in the small and large intestines by premedication with mild aperients, such as "taxol" or vegetable laxatives, and then later thoroughly irrigating the large intestine by the two-way flow colonic lavage technique, using up to, or more than, 50 or 60 pints (28 to 34 l.) of plain water or, if something is specially desired, 1 oz. (28 g.) sodium bicarbonate to the pint (0.6 l.) to break up the mucus. The bowel so prepared is left in its real state, at rest, or, if diseased, perhaps irritable, angry, tired, or exhausted.

These observations should be read in the light they have been written in—not as destructive criticism, but as a help or guide to those who may try to use this drug. In the minority of cases where a mucosal pattern may have been obtained the result is not up to the standard of that produced by the methods of colonic lavage I have briefly outlined above. We have found ethyl methyl cellulose helps to make barium more adherent to the mucosa, using 1 oz. (28 g.) to the pint (0.6 l.) of barium, although this is not entirely satisfactory in all cases.

As I have already stated, veripaque is likely to have a brief life in enema work, and at an early date, like tannic acid, is likely to be on its way out.—I am, etc.,

London, W.1. NORMAN P. HENDERSON.

REFERENCES

1 McLaren, J. W., King, J. B., and Copland, W. A., *Brit. J. Radiol.*, 1955, **28**, 285.
2 Schlegel, L. B., *Die Medizinische*, 1952, 1227.
3 Henderson, N. P., *Lancet*, 1954, **1**, 159.

Treatment of Aphthous Stomatitis

SIR,—I have been recently trying the effect of painting the ulcers in aphthous stomatitis with cyanocobalamin *B.P.* ("cytamen"), with encouraging results. Many are doing the same.

On July 16, 1955, I was called to an 8-year-old boy with a very severe monilia infection of the mouth and pharynx; he was able to open his mouth very little and could not eat. The affected areas were painted with cyanocobalamin every two hours of the day, at a strength of 50 mg. to the ml. To my amazement, within 36 hours the condition had cleared, leaving no trace.

I am wondering if this treatment has been tried with the even more serious types of monilia infections ? Presumably where it occurs in the alimentary tract it could be swallowed; and for bronchitis infections it could be given by an aerosol apparatus. Monilia infections are too rare for me to be able to check the significance of this one case, and I should be glad of any help in evaluating the treatment.—I am, etc.,

Northwood, Middx. DUDLEY M. BAKER.

SIR,—For aphthous stomatitis, of which I have been the victim for many years, I discovered that two doses of intramuscular liver extract on successive days always cured me quickly and in three days.—I am, etc.,

Aix-en-Provence, France. F. ARVOR.

Premenstrual Varicose Veins

SIR,—A woman aged 34 gave a clear symptomatic history which signified varicose veins even before I came to examine her legs. But, to my surprise, the internal and external saphenous systems were completely normal in every respect and there was no sign of any varicosity. Metaphorically scratching my head, I went through her history again and eventually, but with the greatest reluctance on her part, succeeded in obtaining the admission that the aching veins, swollen ankle, and tired leg occurred once a month only, beginning one or two days before menstruation and tapering off with the establishment of the flow. She was instructed to return immediately the symptoms reappeared, and sure enough she then had absolutely typical varicose veins with sapheno-femoral incompetence—which had quite disappeared a week later. I performed a left juxta-femoral ligation and she now has a normal leg.

This happened six years ago, and I am afraid that, apart from making a careful note, I did little more about this supposedly rare fact. But in the intervening time this syndrome has reappeared regularly in my consulting-rooms at least once a year, so that now I have records of seven patients in the 25 to 35 age group with premenstrual varices. And on questioning and calling up for re-examination a number of female patients awaiting operation I have realized that in many cases even fully established varicose veins are more prominent, both objectively and subjectively, in the premenstrual phase.

The main purpose of this communication is to call attention to the fact that there are probably a large number of women complaining of aching tired legs in whom clinical examination, unless fortunately in the premenstrual phase, sheds no light upon the problem. Women seem loth to state that their legs only ache just before their periods—or it may even be that the time connexion is not realized until pointed out by question and answer. But there is no doubt that this can be a real disability and should be looked for more carefully. The aetiology is quite straightforward, and links up with the appearance of varices in the *early* months of pregnancy, long before the uterus is large enough to have, if it ever does have, any direct pressure effect upon the iliac veins. It is due to the increased premenstrual internal iliac venous return which cuts across and dams back that from the external iliac vein.—I am, etc.,

London, S.W.11. STANLEY RIVLIN.

Diabetes and Pregnancy

SIR,—Whenever the subject of therapeutic termination of pregnancy is discussed, differences of opinion inevitably arise concerning the purely medical aspects of the problem. In addition, other issues so often arise—emotional, ethical, humanitarian, and religious—to cloud the judgment and obscure the reason. Had Dr. M. I. Drury said in his letter (*Journal*, August 13, p. 435) that in his opinion there were no indications for terminating pregnancy in any patient, we would accept his view—without agreeing with it—and respect it for what it is. But when he states there is no indication for therapeutic abortion in a diabetic woman he displays a knowledge and experience of the subject and its problems that is either limited in extent or prejudiced by other considerations.

The views expressed by one of us (J. H. P.) at the B.M.A. Meeting in Toronto (*Journal*, July 2, p. 44) this year are views which we have both expressed elsewhere on many occasions. They are based on our experience, over a period of more than 20 years, of several hundred pregnant diabetics, and they are views to which we adhere. As our experience and knowledge grow the more impressed are we by the inherent limitations of the diabetic woman for reproduction, and by the many and varied dangers and complications affecting both mother and child revealed by a more long-term follow-up.

We should like to refer very briefly to three points raised by Dr. Drury in his letter. First, the writings of Priscilla White constantly refer to series of cases "excluding therapeutic abortion." She has, like most authors, wisely avoided any attempt to lay down hard and fast indications, and all that one of us (J. H. P.) attempted to do was to discuss general principles. Secondly, we should like to correct a misapprehension by Dr. Drury of what we mean by a bad obstetric history. We are very constantly seeing patients who have lost one or more babies in previous pregnancies

through a total lack of adequate diabetic control, which Lawrence and Oakley[1] showed in their original paper in 1942 was the most important single factor affecting foetal survival. With proper control they achieve a live baby, as in the case quoted by Dr. Drury. But that is not a bad obstetric history. On the other hand, there are patients who, in spite of the most careful and complete control of their diabetes during pregnancy, produce a row of stillborn babies, often with congenital abnormalities of the grosser type. That is what we mean by a bad obstetric history. The danger of being a potential diabetic is indeed the very least of the hazards to which the fertilized ovum is subjected following its initial nidation in the diabetic uterus.

Lastly, we would like to protest in the strongest possible manner against the implication in Dr. Drury's last sentence that a woman whose "end is near" should have to suffer the added dangers of pregnancy, which, under the particular circumstances to which he refers, has far less than a 50% chance of successful outcome from the foetal point of view. As doctors our function in society is to endeavour to alleviate the pain and suffering of human beings—not to add to them.—We are, etc.,

W. G. OAKLEY.
J. H. PEEL.

London, W.1.

REFERENCE

[1] Lawrence, R. D., and Oakley, W., *Quart. J. Med.*, 1942, **11**, 45.

Treatment of Uterine Bleeding

SIR,—The paper by Barr and Charteris, published in a recent number of the *Journal of Obstetrics and Gynaecology of the British Empire*,[1] should surely impress all who read it with the need for the fuller use of modern methods in gynaecology.

In this most comprehensive paper 850 case papers were analysed covering a period of 22 years, in order to determine whether the cure of simple uterine bleeding by intrauterine radium was as satisfactory as hysterectomy, bearing in mind the need to reduce long waiting-lists and the rising cost of the hospital services. In studying these cases it was found that: (1) Every patient had at least 1 week in hospital, 5% had one or more further treatments, and 15 had immediate post-operative complications. (2) The number of cases between the ages of 31 and 50 was 729, representing more than 85% of the total. (3) Pelvic examination showed 82% had no detectable abnormality, or only a very slight enlargement of an apparently normal uterus. 15.2% had enlarged or cystic ovaries. (4) Histological reports showed 54.2% had no abnormality whatsoever. Of those with recognizable pathology, 27.1% showed some degree of cystic glandular hyperplasia.

From examination of these figures it would appear that in a great many of these cases there was no need for surgery. Such cases can be treated successfully by well-established endocrine therapy, which will produce symptomatic relief by physiological control of the bleeding, which is surely to be preferred to the destructive action of radium or major surgery.

In these days of domestic difficulties, pressure on hospital beds, and the general economic problem, surely it is a retrogressive approach to determine which of two operations will prove the more satisfactory, before one has used the very potent and reliable hormones now at one's disposal, which do not necessitate in-patient treatment.—I am, etc.,

SARA FIELD-RICHARDS.

London, W.1.

REFERENCE

[1] Barr, W., and Charteris, A. A., *J. Obstet. Gynaec. Brit. Emp.*, 1955, **62**, 187.

Neurosis in General Practice

SIR,—Dr. J. C. E. Pougher is to be congratulated upon the admirable way in which he has presented (*Journal*, August 13, p. 409) his arguments for the recognition and treatment of "Neurosis in General Practice." He has disproved the customary gibe that those who are interested in neurotic illness are apt to be unscientific and not sufficiently statistically conscious in reporting their observations. My own interest in the neuroses started with general practice over 50 years ago, and it may be of interest to record that for a period during the last war, whilst waiting for a more specialized appointment, I took a "refresher course" by doing locum work for general practitioners.

I soon found myself in a dilemma, the horns of which were on the one hand my loyalty to my principal and paymaster, and on the other my recognition of the fact that many of his regular patients required nothing but elucidation of their emotional problems and reassurance. I used to say (in private) that given a free hand I would engage to diminish the practice of any G.P. by at least a third. Now that the Health Act makes such an approach more feasible it is to be hoped that many will be willing to learn from Dr. Pougher.

The sex drive is the most repressed and readily distorted of all instinctive drives, and it is only to be expected that, as Dr. Pougher found, most of the anxiety which undermines the health of the individual stems from that source. In this connexion I should like to put in a plea for a positive attitude towards masturbation, in place of the usual negative. It is, I hope, sufficiently realized now that the obsessive masturbator is the victim of a vicious circle in which anxiety, not sensuality, is the prime factor. Remove his anxiety by the definite assurance that he has not done, nor can he do, himself any harm, and he regains his self-control and happiness. It is, too, the guilt-engendered anxiety which is the commonest cause of ejaculatio praecox, as well as of other types of marital failures.

In the nature of things I have no statistics to offer, but it seems reasonable to suppose that recognition of masturbation as a permissible activity, when pent-up libido craves an outlet, may prevent the tragic regressions of elderly widowers and bachelors to exhibitionism and child molestation. I believe, too, that there are homosexuals whose bias could be sufficiently controlled if they were able to break away from the superstitious social taboo on solitary indulgence and thus provide themselves with a safety valve without anxiety or regrets.—I am, etc.,

R. MACDONALD LADELL.

Scarborough.

Reflex Renal Ischaemia

SIR,—Drs. Barry, Feeney, and Geoghegan (*Journal*, July 2, p. 12) have produced sufficient evidence to infer the existence of the stretch stimulus by the success attending rupture of the membranes in concealed accidental haemorrhage, and have shown that renal ischaemia is its reflex manifestation, since anaesthetic "renal denervation" overcomes early anuria, presumably by re-establishing the blood flow to an ischaemic organ.

Their data should be considered side by side with those who, by employing conduction anaesthesia in the termination of pregnancy both in eclampsia and in severe pre-eclampsia, secured dramatic recovery, including the early relief of oliguria, when the anaesthesia reached the level of the lesser splanchnic nerve.[1-16] It may be inferred, therefore, that renal ischaemia is aetiologically significant both in toxaemia and in anuria, or threatened anuria, complicating accidental haemorrhage, and that distension of the uterus plays a determining role by reflexly provoking it. The experimental evidence provided by Byrom,[17] of inducing encephalopathy by renal ischaemia in rats and securing recovery by removal of the renal clamp, helps to increase our understanding of the mechanism underlying eclampsia and its relief by conduction anaesthesia—the equivalent of removal of the renal clamp. The clamped kidney was free from vascular damage, a fact of considerable importance for fuller consideration later.

Renal research denies the inference that ischaemia of the kidney in toxaemia is due primarily to generalized vasospasm even though it shares in it. Experimental hypertension persists if during the vasospastic process the kidney suffers vascular damage, for this supervenes on the hypertension unless the calibre of the renal artery has been concurrently reduced by the use of a clamp. Freedom from

hypertension subsequent to recovery in eclampsia, unless based on essential hypertension, consequently strongly indicates a protective spasm of the renal artery, whilst a shut-down of its intralobular branches has been amply demonstrated by Sheehan and Moore[18] in anuria where hypertension is not a sequel either. While the severe eclamptic can on occasion become anuric, a fact not so well known is that the anuric patient, if injected intravenously with normal saline, develops oedema, hypertension, and fits. Albuminuria in any case is an accompaniment of this form of renal failure.[19]

It is highly significant, therefore, in connexion with the aetiological problem, to find that the shut-down kidney, whose existence in anuria is undeniable, can in association with intravenous sodium become responsible for the production of hypertension. It would appear both in eclampsia and anuria that a renal ischaemia obtains. Goldblatt[20] showed that partial clamping of both kidneys in the dog, although responsible for a generalized vasospasm, protected these organs from vascular damage, provided the reduction in blood flow had not provoked renal failure. Wilson and Byrom[21] demonstrated that unilateral renal arterial constriction brought about a sustained hypertension; that the clamped kidney escaped vascular damage; that hypertension was sustained even though the clamped organ was removed; and that the unclamped organ regularly displayed vascular damage, to which change the maintenance of the raised blood pressure was held to be due. Persistence of hypertension after removal of the ischaemic (clamped) kidney in rats has also been confirmed.[22,23] Byrom and Dodson[24] have provided a counterpart to clinical recovery from toxaemia by demonstrating that hypertension due entirely to the persistence of renal ischaemia could be recovered from if the normal blood supply to the organ was re-established. They evoked hypertension in rats by constriction of one renal artery, and thereafter the opposite kidney was removed. This hypertension, entirely attributable to renal ischaemia, was allowed to persist for 12 weeks, when the clip on this, the sole remaining kidney, was removed. Thereafter the raised blood pressure fell to normal limits within 12 hours. Once again the clipped kidney, on subsequent examination, proved to be free from vascular lesion. Floyer[25] confirmed this return to normality of the blood pressure when based purely on renal ischaemia and when vascular lesions of the kidney could be excluded.

The aetiological problem of hypertension in toxaemia has a counterpart in experimental renal hypertension primarily due to ischaemia of the kidney. Reversibility of hypertension denies the existence of renal vascular damage, from which the kidney is protected as a result of clamping. The Trueta changes in renal circulation provide for the reduction in the calibre of the renal artery. No renal humoral pressor substance (arising because of renal ischaemia) has so far been shown to affect vessels of the size of the renal artery. The evidence suggests that an Oxford mechanism can best explain the hypertension of toxaemia, and is against the view that a generalized vasospasm initiates the process; also that conduction anaesthesia can be interpreted as producing denervation of the kidney, protecting it against the utero-renal reflex.—I am, etc.,

London, W.1. J. SOPHIAN.

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Detecting Non-agglutinating Antibodies to the Tubercle Bacillus by Coombs's Test

SIR,—Since Middlebrook and Dubos[1] demonstrated that concentrated aqueous extracts of tubercle bacilli could be adsorbed on the surface of human erythrocytes to give an agglutinable antigen, the method has been used as a diagnostic aid in tuberculosis. Some questions have been raised as to the specificity and reactivity of the test, especially with respect to its ability to yield positive results in all cases of proved active tuberculosis.

The value of a serological test using the patient's serum offers much to the study of tuberculosis. The present author has been interested in such data from the viewpoint of the immune antibody globulins and their activity.[2,3] The methods for detecting ABO blood group and anti-CDE/cde erythrocyte agglutinins, agglutinoids (blockers), and cryptagglutinoids ("incomplete" antibodies) were applied to the Middlebrook–Dubos test. The method most useful in our studies has been the Coombs test.[4] We have applied the Coombs anti-human globulin serum to the haemagglutination titrations of 63 proved cases of tuberculosis. In 8 of these cases the Middlebrook–Dubos test showed negative results, 31 gave titres between 1/2 and 1/16, while 24 revealed titres ranging from 1/32 to 1/512. When the test for cryptagglutinoids using the Coombs reaction was applied, all 63 sera showed positive results. Four of the sera had titres of 1/2 to 1/16, and the remaining 59 sera ranged from 1/32 to 1/1024.

The application of the Coombs technique gives evidence of increased sensitivity for serological testing for tuberculosis antibodies in that the method includes the cryptagglutinoid as well as the agglutinin. The antibodies thus found show characteristics similar to those demonstrated in the case of iso-immunization to erythrocyte antigens, especially those of the anti-CDE varieties.—I am, etc.,

Dallas, Texas. SOL HABERMAN.

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Treatment of Tuberculosis

SIR,—Your otherwise comprehensive annotation (*Journal*, August 13, p. 424) omits one important development in this field: ambulant chemotherapy. The need for long-term drug treatment, to continue many months after discharge from hospital as fit for work, has led to the common practice of sending the bread-winner off each morning with a bottle of *p*-aminosalicylic acid in one pocket and a handful of isoniazid tablets in the other, perhaps calling in on the factory nurse for a shot of streptomycin in his lunch-hour.

As chemotherapy while doing a full day's work presents little practical difficulty, we now use it from the Windsor Chest Clinic in some cases without preliminary bed rest or hospitalization. We agree that bed rest is necessary where disease is acute or where toxaemia is present. Much of its value in cavitary lesions probably derives from posture rather than rest *per se*. Indolent apical lesions of haematogenous or acinous-nodose type are probably not much influenced by rest, but often clear up under drugs.

The psychological and economic advantages of retaining a good job must be weighed against the questionable results

of immobilization. We have treated a few dozen patients so far without apparently doing any harm and usually with as good a result as could have been expected under a full sanatorium regime. In some the treatment has been preventive, where the lesion is threatening but not definitely active. Such cases form an increasing proportion of chest clinic practice, often coming to us from mass radiography. Doubtless some of them would be all right without treatment at all, but we feel that any error is on the right side and the patient is at any rate no worse off. The emergence of resistant strains of organism is theoretically a risk that we have to take.

As you so rightly point out, assessment of results of any treatment is difficult, and of prophylactic treatment impossible. I cannot see us publishing any useful figures, but I think it right to draw your attention to this work, which is, I dare say, no more than is done by many chest clinics elsewhere. May I finally assure you that ambulant chemotherapy while at work is applied only where tubercle bacilli are not being excreted.—I am, etc.,

Windsor. BRIAN C. THOMPSON.

The Mysterious Granuloma

SIR,—I read with interest the annotation on "The Mysterious Granuloma" (*Journal*, August 20, p. 481). It seems to me that the importance of early radiotherapy in this condition was not sufficiently stressed. Apart from the recently reported cases successfully treated by radiotherapy to which reference was made, I have myself had two cases, and probably a third, in all of which the response to deep *x*-ray therapy in quite moderate dosage was dramatic and complete. One of these cases is pictured in my *Handbook of Radiotherapy*.[1] This was a boy of 11 who had had repeated and ever-wider excision of his nose and upper lip before coming under observation by me, to be followed inevitably by recurrence. Complete healing was obtained by radiotherapy within a month, but the loss of tissue as a result of the excisions was considerable. Undoubtedly a much better cosmetic result could have been obtained had the patient been submitted to radiotherapy in the first instance.—I am, etc.,

London, W.1. WALTER M. LEVITT.

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Diet in Acute Nephritis

SIR,—In your leading article (*Journal*, August 13, p. 423) consideration is given to the question of the dietary protein in acute nephritis. A further much-discussed question has relation to the fluid intake in that condition. In accordance with one view, large quantities of fluid should be given during the early stages, with the object of diluting the concentration of sodium chloride and promoting its excretion. These ideas appear to have been justified by the clinical results, but it would be interesting to know how far they hold good at the present time.—I am, etc.,

Sheffield, 10. R. G. ABERCROMBIE.

The Late Lord Horder

SIR,—The members of our family have been very much touched and pleased by the obituary notice and personal tributes which you recently published in honour of my father, the late Lord Horder, and we should like to express our thanks to you.

I want, in course of time, to put together a short memoir of my father's sayings and doings as his friends remember them, believing that he would have preferred this to a more formal full-length biography. It would be very helpful to me if doctors or nurses or others who have any detailed memories of him, at work or play, could find time to jot them down, date them, and send them to me. I am particularly interested in the first 50 years of his life, down to 1920. Any interesting letters will be copied and returned.—I am, etc.,

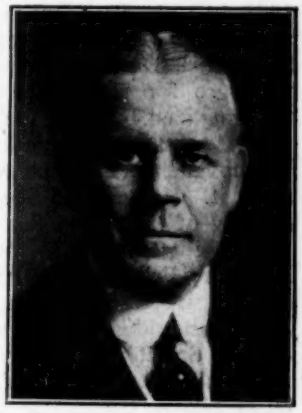
Ashford Chace,
Petersfield, Hants. HORDER.

Obituary

Sir JAMES WALTON, K.C.V.O., M.S., F.R.C.S.

A figure greatly respected, who for forty years occupied a prominent position in British surgery, is taken from us by the death of Sir James Walton on August 27 at the age of 73. Many generations of London Hospital men came under his influence. As student and as active member of the staff he was identified with the London for almost half a century, and he will be remembered as the embodiment of the best surgical traditions, a careful and illuminating teacher, and a most kindly chief and colleague.

He had a store of reminiscences, mostly concerned with the great East End Hospital and the great men who served it, and on these he used to draw at medical meetings, but never to the weariness of his audience. He expressed his views always firmly and precisely, but never intolerantly. His favourite theme was the importance of surgical diagnosis, and if he felt that younger men were stressing too much the value of laboratory examinations nothing could be better than his reminder that the first need, whatever came second, was clinical diagnosis. He was a great surgical diagnostician, and one of his anxieties was that surgical diagnosis might be outstripped by the knowledge and practice of operative treatment. He was accustomed to say that it was in diagnosis that the weakness of modern surgery lay, and to point out that it was more difficult to determine when and how to operate than to carry out the technical details of the operation.



[*Elliott & Fry*

Albert James Walton was born in London on November 1, 1881, and educated at Framlingham College. From there he went to the London Hospital Medical College, taking his M.R.C.S., L.R.C.P. in 1905, his B.Sc. of London University with honours in anatomy and morphology in 1906, and his M.B., B.S. of London with honours in pathology, midwifery, and gynaecology in 1908. He had already taken his F.R.C.S. in 1907 and he followed this with the M.S., London, in 1909. His student career was brilliant, and he took no fewer than six scholarships at the London Hospital, including the scholarships in medicine, surgery, and obstetrics.

With these qualifications and achievements he was well set for the distinguished career in surgery that followed. He began by holding several house appointments at the London—emergency officer, house-physician, receiving room officer and resident anaesthetist, house-surgeon, assistant director of the pathological institute, surgical registrar, and demonstrator in anatomy. In 1913 he was elected to the surgical staff and held the position of surgeon until his retirement in 1946, when he became honorary consultant. Other hospital appointments which he held were those of consulting surgeon to the Victoria Hospital, Kingston-upon-Thames, where he served from 1920 onwards; and

surgeon to the Poplar Hospital for Accidents, the Evelina Hospital for Children, and the Seamen's Hospital, Greenwich.

In the first world war he was captain R.A.M.C., stationed at the 2nd London General Hospital, and he also served at the Endsleigh Hospital for Officers, the Empire Hospital for Diseases of the Brain and Spinal Cord, and the Palace Green Hospital for Officers. In the second world war he was attached to the Army Medical Department with the rank of brigadier. In 1930 he was made surgeon to the household of George V and remained in that position during the two succeeding reigns until 1949, when he became extra surgeon. He was also surgeon to Queen Mary from 1936 to 1949 and extra surgeon from 1949 to 1953.

Walton was a prominent figure at the Royal College of Surgeons of England. As far back as 1919 he had been Hunterian Professor, and later he was a member of the Council of the College and Vice-President. In 1943–4 he was President of the Association of Surgeons and in 1946 President of the Medical Society of London, in which last body he was perhaps most at home. It was rare for a Monday evening discussion to pass unilluminated by some remark from him, though at his request most of his remarks were "off the record," and perhaps all the more pointed and enlightening on that account. He had also filled the chair of the Section of Surgery of the Royal Society of Medicine. His reputation went beyond this country. In 1936 he was made Honorary Fellow of the American College of Surgeons, and he was also an Honorary Member of the Inter-State Postgraduate Association of America, a member of the Société Internationale de Chirurgie, and the Académie de Chirurgie of Paris. He was an Officier de la Légion d'Honneur, and in 1935 he was created Knight Commander of the Royal Victorian Order.

Many papers on surgical subjects came from his pen and at least two textbooks, one on the surgical dyspepsias and the other on surgical diagnosis. He had published an earlier work on fractures and separated epiphyses. For his work on surgical diagnosis he enlisted the help of some thirty authoritative writers and himself wrote the chapters on diseases of the pituitary gland, of the thyroid and parathyroid, of the liver, gall-bladder, and bile ducts, lesions of the stomach and duodenum and of the abdominal wall, injuries and diseases of the pancreas, and visceroptosis, thus indicating his own special fields of interest. The work was first published in 1928 to enable students, as he said, to keep abreast of the voluminous literature of modern surgery.

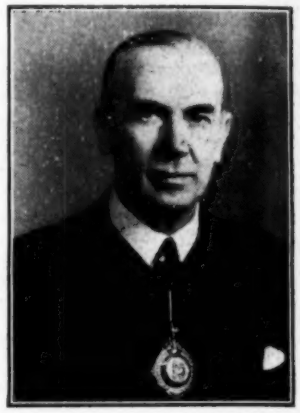
His recreations were fishing, tennis, and badminton. He was also an expert on precious metals and gems, being a Fellow and Chairman of the Gemmological Association and President of the Association of Goldsmiths. He was twice married; by his first wife, Nancy Mary Trevett, who died in 1953, he had one son, also in the medical profession, and one daughter. In 1953 he married Renée Carrington, who survives him.

We are indebted to Sir HENRY SOUTTAR for the following appreciation:

The passing of James Walton closes a friendship which began more than fifty years ago, when we were students at the London Hospital together, and which deepened with the passing years, during which we were colleagues on the surgical staff. He was some two years my senior in medical standing, and I well remember his alert, vivid personality, and his apparently unlimited knowledge of medicine and surgery. He carried off every available prize with facility, and almost as an afterthought he took the London B.Sc. with honours while holding a house appointment. He was a brilliant teacher, and many of us owed much to the incisive clarity of his demonstrations. I had the good fortune to serve with him as a surgical registrar, and I was able to watch from its early beginnings the gradual development of his technique. He became a very great surgeon, and there are few who have added more to the lustre of British surgery. He was also a very great gentleman, and to those of us who knew him well that is the aspect of his achievement which we would most wish to remember and for which in our hearts we are most deeply grateful.

ANDREW TOPPING, C.M.G., T.D., M.D.,
F.R.C.P.Lond., F.R.S.Ed., D.P.H.

A career of distinction in many fields of public health and social science is brought to a close with the greatly regretted death on August 28, at the age of 64, of Andrew Topping, Dean of the London School of Hygiene and Tropical Medicine. Topping was not only a first-class administrator, with experience in the international as well as the national field, but one who could be called a statesman in public health, a man of vision, and one able to put forward his views, which were sometimes contrary to those of the majority of his profession, with courage and clarity. The public health world and many other fields of activity will long miss his highly individual personality, his forthright speech, and his kindness and helpfulness to colleagues and students.



[*Elliott & Fry*

Andrew Topping was born on December 20, 1890, the son of Robert Topping, an inspector of schools in the Scottish Education Department. He was educated at the Robert Gordon College and at Aberdeen University, taking his M.A. in 1911 and the M.B., Ch.B. degrees in 1914. At the beginning of the first world war he entered the R.A.M.C. and served until 1919 in France, Gallipoli, and Mesopotamia, where he was officer in charge of the medical division of No. 3 British Hospital and was mentioned in dispatches. Afterwards he was officer in charge of the 5th London General Hospital, holding the rank of Lieutenant-Colonel, R.A.M.C., T.A. He retained his connexion with the Territorial Army and received the Territorial Decoration in 1933. After the first world war he saw some further overseas service as senior medical officer with the Anglo-Persian Oil Company at Abadan. He took his M.D. (with commendation) in 1923, and his D.P.H. in the same year. He became F.R.C.P.London in 1946. He was elected a Fellow of the Royal Society of Edinburgh in 1938. In 1954 he was appointed C.M.G.

His services in the public health field in this country began in 1923 at Woolwich, and afterwards he served the County of Lancashire as an assistant medical officer. In 1930 he then became medical officer of health for Rochdale County Borough. Coming back to London in 1932, he entered the service of the London County Council as medical superintendent of the Southern Convalescent Fever Hospital at Dartford, and afterwards was deputy medical officer of health and schools medical officer for London county. In 1942 he was given special charge

of the direction of the ambulance service. With this work he combined that of lecturer in public health at Charing Cross Hospital Medical School. He was also then or later examiner for the D.P.H. for the English Conjoint Board and examiner in hygiene for the University of London.

His great work in the second world war was associated with U.N.R.R.A. (United Nations Relief and Rehabilitation Administration), where he was deputy chief of the relief services and formerly director of the European health division. U.N.R.R.A. began its work in November, 1943, and passed into history after two years or more with a record of accomplishment in public health on an unprecedented scale, and with results of vital importance for the world. Medical and sanitary supplies were provided in great abundance, national health departments were resuscitated, epidemics were prevented or arrested, and the aided countries supported on the way to recovery. In a memorable address to the Royal Sanitary Institute in 1946, Topping described the work which had been done and gave a picture of the administration of U.N.R.R.A. from the head directorate in Washington, through the European regional office, to which he was attached, and thence to the various field missions. The work was one which enlisted his enthusiasm and revealed his statesmanlike qualities.

Another great piece of work which he undertook towards the end of the second world war was, on the instruction of the Minister of Health, the preparation of the report on hospitals for London and the surrounding counties—an area extending from Dorset to Bedfordshire. This report, in which he was associated with Sir Archibald Gray, was published in 1945, and ran to some 80 large text pages of a Blue Book, with 150 further pages of tables.

In 1950 Topping was chosen to succeed Professor J. M. Mackintosh as dean of the London School of Hygiene and Tropical Medicine, vacating the chair of social and preventive medicine at Manchester, which he had occupied since 1947, to accept the new appointment. When he submitted the report of his first year as dean he spoke of several new developments, among others the attachment of students to rural as well as to metropolitan and surburban communities as part of their studies in the public health field; an intensive investigation of health conditions in an area of the home counties in which students from the school were associated with officials from the local authorities; and finally the formation of an association of old students. He proved to be during the whole of his deanship a very active and progressive leader.

Andrew Topping published many articles in the professional journals, on fevers (which was his specialty), on maternal mortality, on hospital administration, and on European health problems, of which he had an unusual experience. He also wrote the article on hospitals in the latest edition of *Chambers's Encyclopaedia.*

He was a Fellow and Member of Council of the Royal Sanitary Institute (now renamed the Royal Society for the Promotion of Health) and in 1952 was unanimously elected President of the Society of Medical Officers of Health, having been previously President of the Fever Group of that society. His presidential address made some stir when he urged that more money should be spent on prevention, that expenditure on sanitoria might be more effectively used in educating the people in the prevention of tuberculosis. Topping was a strong supporter of the medical officer of health, and he felt that local authorities had never received adequate gratitude for what they had done in the development of hospitals during the period between the passing of the Local Government Act, 1929, and the National Health Service Act, 1946.

On one public occasion he protested against the "stranglehold of consultants." Because a man did not want to do general medicine, feeling that he had not the right philosophical or psychological approach, and decided instead to be an expert in allergy or anaesthetics, was it any reason, asked Topping, why he should be looked upon as an entirely different and superior person?

Of the National Health Service on its initiation he declared that it was the most comprehensive legislative effort of all time in the field of health. Later, after some years' experience of the Service, he said that the British people seemed to be becoming a race of hypochondriacs, with a considerable mixture of frank malingerers.

He had always declared himself in favour of a salaried service, and although, he said, the profession as a whole had violently opposed that view, he believed that more and more the thinking element were beginning to realize that the advantages would far outweigh the disadvantages and that where such a service was introduced it would immediately remove many of the difficulties which now beset the Service. He added the remark—this was in 1949—that if we were still demanding more hospital beds ten years after that date our health service must be voted a failure. He served as chairman of the Archway Group Hospital Management Committee from 1952 to 1955. A member of the British Medical Association for 36 years, he served as a vice-president of the Section of Public Health and Hygiene when the Association held its Annual Meeting at Aberdeen in 1939, and at the Dublin Meeting in 1952 he was president of the Section of Social Medicine and Occupational Health. He was elected an honorary Fellow of the American Public Health Association in 1954.

Andrew Topping often declared against the habit of looking upon money as the one thing that mattered. He said that there were many things which were more important, such as happiness in one's job. He had supreme happiness in his own job, or many jobs, but he had great domestic happiness as well, and much sympathy will be extended to his widow and to his son and daughter.

J. M. M. writes: When Andrew Topping came to the London School of Hygiene and Tropical Medicine as dean in the spring of 1950 he brought with him an exceptionally wide knowledge of men and affairs. From his student days he had been an attractive public speaker, a lover of his kind, and an excellent mixer. He was never fond of anything that could be described as highbrow and was apt to conceal his good knowledge of the classics. During the greater part of his career, spent in the service of the London County Council, Topping earned a fine name for himself in his knowledge of both public health and infectious diseases. The war brought out his great administrative talents and his remarkable aptitude for ordered thinking. It was in the years 1942–3 that he carried out, on behalf of the Ministry of Health, a brilliant survey, in collaboration with Sir Archibald Gray, of the hospitals of London and Southern England. To a man of his eager temperament even service in London was not sufficiently broad wartime experience. He was appointed director of the health division of U.N.R.R.A. in 1944, and a year later he was promoted deputy director general in charge of the relief services. During this period he used his talent for organizing to great effect and made many friends throughout the world who will remember him with admiration.

He was the first full-time Dean of the London School of Hygiene and Tropical Medicine. Characteristically his main interests were in developing the world-wide associations of the School and in forging stronger links between ex-students and their teachers. He was instrumental in forming the School Association, which has held several annual dinners under his cheerful presidency. Andrew Topping was in fact a robust speaker; he was a great connoisseur of stories, which he told with immense gusto and success. As President of the Society of Medical Officers of Health in 1952 his personality was a revelation of good nature, and his friendships were firm and loyal. It was always fun to go and have a talk with him over a glass of sherry.

E. C. HODGSON, D.S.O., M.R.C.S., D.P.H.

Colonel E. C. Hodgson died at his home at Henley-on-Thames on June 17 at the age of 76. He had had a distinguished career in the Indian Medical Service, in which he served for over 30 years.

Ernest Charles Hodgson was born in India on October 22, 1878, the third son of Colonel George Hodgson, of the Indian Staff Corps, and was educated at the old United Services College, Westward Ho, where he won many prizes for athletics. Coming of a family associated with the Indian Services, but debarred by myopia from entering a combatant regiment, he enrolled at St. Bartholomew's Hospital as a medical student in 1897, and qualified M.R.C.S., L.R.C.P. in 1902, taking the Cambridge D.P.H. seven years later.

After qualification he held the appointment of resident clinical assistant at St. Luke's Hospital, London. He entered the Indian Medical Service as a lieutenant in 1904, and served in India until the outbreak of the first world war in 1914. From then until 1918 he was in command of the Ambala Cavalry Field Ambulance in France and Flanders, later going with the unit to Palestine, where he was present at the final battle of Megiddo. In 1918–19 he commanded the 5th Cavalry Field Ambulance in Egypt, and subsequently became A.D.M.S. of the Egyptian Expeditionary Force. For his war services he was twice mentioned in dispatches, and in 1918 was awarded the D.S.O. On his return to India Hodgson was employed for a few years at the Bombay Bacteriological Laboratory, and among later appointments he was director of the Pasteur and Medical Research Institute at Shillong, Assam, A.D.M.S. of the Deccan district, and Assistant Director-General of the I.M.S. He was one of those consulted about the site of New Delhi. From 1929 to 1935, the year of his retirement from the I.M.S., he was an Honorary Physician to the King, and in the latter year was awarded King George V's Silver Jubilee Medal. Hodgson's integrity, loyalty, and kindliness won him many friends, and his ability was shown by his appointment to many important posts. He married Miss Guelda K. Earle, who predeceased him. They had one son, Captain Robert Hodgson, R.E.

LORD HORDER OF ASHFORD
G.C.V.O., M.D., D.C.L., F.R.C.P.

Dr. C. B. HEALD writes: I am not going to make any attempt to add to your eloquent, or Sir Henry Dale's touching, memoir of Lord Horder (*Journal*, August 20, p. 493, and August 27, p. 565). As my memory of this delightful and mercurial Puck of Medicine is almost as long as Sir Henry's, and as the only surviving medico of the (almost notorious) committee of inquiry into the claims of the Abrams box, I will content myself with three silhouettes covering these last 35 to 40 years.

When "Tommy" obtained, not without some difficulty, a platform at the Royal Society of Medicine for the presentation of the committee's report on the Abrams box, the majority of the Press notices in the medical journals were highly critical of his participation in the inquiry at all, and also of the committee's findings. This was an injustice that he took uncomplainingly with a shrug, but it should now be remedied. His whole attitude from the beginning was, "Let us find the truth, the whole truth, and tell it to the medical world fully and fearlessly." When the tests were completed he called together the exponents of the famous box and explained to them that it was first and last a complete fake. It had been a condition of the inquiry that the committee would promise not to break the seals of the box, but would conduct their tests entirely clinically. This did not prevent the committee having *x* rays taken of the box, which showed beyond all doubt that it was a fake. The exponents were, of course, badly shaken and threw themselves on Horder's mercy. He, recognizing that this cult was already dying and would, indeed, shortly be dead, toned down the committee's final draft rather than expose and hurt well-intentioned but duped brother professionals.

Another 20 years and the scene is the British Legion unit of rheumatology at Arlesey, and the occasions are "the Horder round." These rounds, which he and all the students and postgraduates who crowded to them enjoyed intensely, showed him as recently as 1946 a master of his art. But woe betide the questioner who tried to catch him out. My last little picture is as recent as the end of June this year. In this lovely Cotswold village of Chipping Campden, right in the main street, is our unpretentious house, but pass through it and there expands a garden of surpassing beauty lovingly cared for by the octogenarian owner and his wife. "Tommy" is strolling across the lawn, his arm round my wife's shoulder while she leads him to a sick tree. One look, and unhesitatingly he prescribes for the patient. The remedy recommended is immediately applied, and to-day "the patient is quite recovered and doing very nicely, thank you." How it would have delighted him.

Dr. DAVID PYKE writes: Lord Horder was sometimes thought to have given his name to too many societies. But what is seldom mentioned is the appreciation of the many associations he befriended. Members of the Family Planning Association, whose President he was since its foundation in 1930 until the day of his death, will never forget him. It needed some courage 25 years ago even for a man as eminent as Lord Horder already was to take the part of a body engaged in spreading knowledge of family spacing and the relief of infertility. But neither then, nor at any other time, was his help wanting at times of crisis. His authority and experience enabled the Family Planning Association, as doubtless it did other societies, to develop quickly and soundly. He will be much missed.

Vital Statistics

Poliomyelitis

The incidence of acute poliomyelitis in England and Wales remains above average, though the 348 cases in the week ending August 20 were 10 fewer than in the previous week. The paralytic cases, 198, numbered 4 more than in the previous week, and the non-paralytic, 150, were 14 fewer. In the great towns 13 deaths were registered, as compared with 8 in the previous week and 4 in the week before that. The total number of uncorrected notifications from the beginning of the year to August 20 is 2,226, as compared with 1,252 in 1954, 2,845 in 1953, 2,169 in 1952, 1,631 in 1951, and 3,536 in 1950.

The rates at the following places are above the average; figures are for cases notified by August 20 (with incidence

per 100,000 population in parentheses): Barnsley C.B. 70 (93.4), Hoyland Nether U.D. 11 (69.4), Dover M.B. 19 (55.8), Wombwell U.D. 8 (47.8), Stepney M.B. 46 (47.0), Willesden M.B. 80 (45.1), Thurrock U.D. 40 (41.2), Poplar M.B. 27 (37.6), Worsborough U.D. 5 (34.8), Wisbech M.B. 5 (29.1), and Aylesbury R.D. 8 (25.3).

In London non-paralytic cases continued to exceed paralytic, and this occurred also in 16 counties. Elsewhere the ratio is more as in former years.

Outbreak at Royal Free

The infectious disease of unknown origin which has recently been prevalent among the staff of the Royal Free Hospital continues to wane, but in the week up to August 30 some cases were reported for the first time at the Lawn Road branch. These comprised 5 nurses, 1 patient, and 2 non-medical staff; total 8. The outbreak there has shown none of the explosive spread which characterized it in its early stages at the Gray's Inn Road branch.

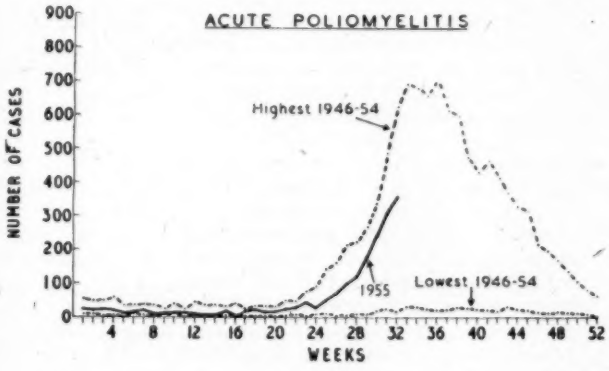
Industrial Accidents and Diseases

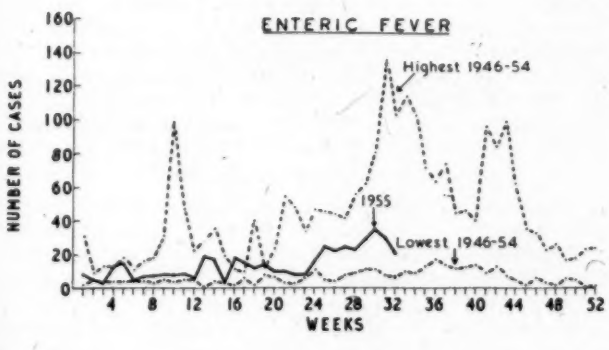
The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in July was 105, compared with 104 (revised figure) in the previous month and 96 (revised figure) in July, 1954.

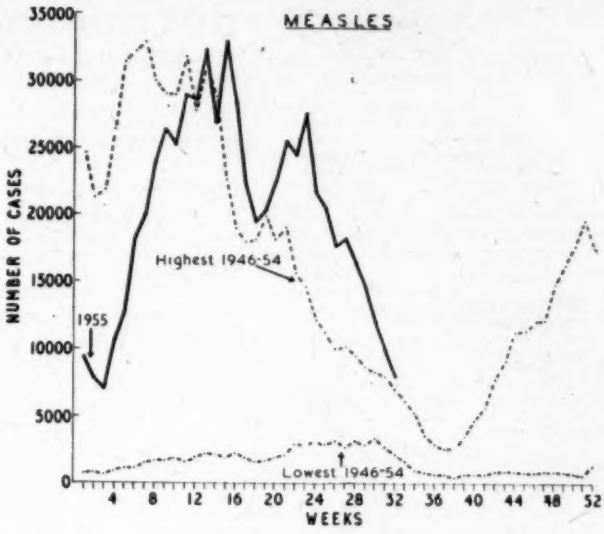
The numbers of cases of industrial diseases in the United Kingdom reported during July, 1955, were as follows: lead poisoning 6, anthrax 4, epitheliomatous ulceration 10, chrome ulceration 23, total 43. There were no deaths—*Ministry of Labour Gazette*, August, 1955.

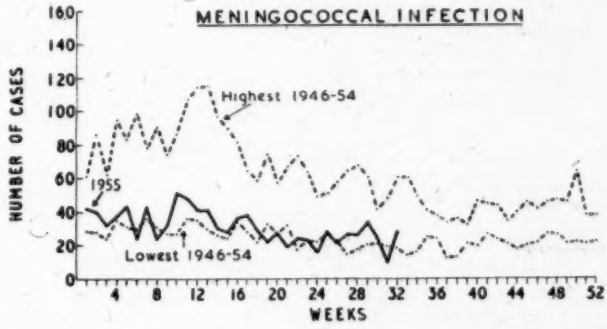
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1946–54 are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The largest fluctuations in the trends of infectious diseases in England and Wales during the week ending August 13 were a fall of 1,883 in the number of notifications of measles, from 9,971 to 8,088, and rises of 307 for whooping-cough from 1,553 to 1,860, 51 for acute poliomyelitis, from 307 to 358, and 38 for scarlet fever, from 196 to 234.

The largest falls in the incidence of measles were 169 in Southampton county, from 579 to 410, 153 in Bedfordshire, from 257 to 104, 153 in Kent, from 639 to 486, 148 in Lincolnshire, from 337 to 189, 138 in Yorkshire West Riding, from 426 to 288, and 126 in Devonshire, from 414 to 288. A small increase in scarlet fever was recorded in most regions. The largest rises in the number of notifications of whooping-cough were 62 in Bedfordshire, from 20 to 82, 57 in Warwickshire, from 81 to 138, and 48 in Essex, from 55 to 103. 4 cases of diphtheria were notified, being 1 fewer than in the preceding week. Two of the cases were notified in Manchester C.B. This is the second occasion when only 4 cases of diphtheria have been notified in one week.

373 cases of dysentery were notified during the week, and this total was 19 fewer than in the preceding week. The largest centres of infection were Lancashire 81 (Liverpool C.B. 26, Blackpool C.B. 10, Manchester C.B. 10), Yorkshire West Riding 62 (Huddersfield C.B. 21, Leeds C.B. 21), London 58 (Southwark 18), Durham 28 (South Shields C.B. 9), and Yorkshire North Riding 17 (Middlesbrough C.B. 12).

In Scotland the notifications of dysentery increased from 140 to 193, of which 136 were notified in Glasgow.

Week Ending August 20

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 234, whooping-cough 1,684, diphtheria 3, measles 5,567, acute pneumonia 202, acute poliomyelitis 348, dysentery 284, paratyphoid fever 17, and typhoid fever 2.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **August 13** (No. 32) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	4	1	4	0		7	2	8	1	0
Dysentery	373	58	193	10	5	384	66	113	0	9
Encephalitis, acute	4	0		0		5	0	0	0	
Enteric fever:										
Typhoid	2	0	1	2		4	0	0	1	
Paratyphoid	19	2	3	0	1	15	3	0	0	5(B)
Food-poisoning	371	30		3		181	20		0	
Infective enteritis or diarrhoea under 2 years				18	26				10	19
Measles*	8,088	124	33	40	64	2,840	123	46	87	102
Meningococcal infection	28	9	17	2	1	35	1	7	3	1
Ophthalmia neonatorum	33	4	5	0		26	1	3	0	
Pneumonia†	194	7	101	5		279	11	71	2	0
Poliomyelitis, acute:										
Paralytic	194	29	25	0	3	60	2	22	4	3
Non-paralytic	164	38				37	2			
Puerperal fever§	199	31	12	2		252	31	18	1	
Scarlet fever	234	23	28	11	5	431	24	69	11	19
Tuberculosis:										
Respiratory	604	85	101	18		670	61	88	21	
Non-respiratory	93	5	8	4		104	11	9	7	
Whooping-cough	1,860	82	75	88	106	2,090	92	134	10	45

DEATHS in Great Towns	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	1	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	1	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	3	0	0	2	1	8	0	3	0	1
Influenza	3	0	0	0	0	3	0	1	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		1	0				1	0		
Pneumonia	119	24	16	10	2	122	22	14	8	5
Poliomyelitis, acute	8	2			0	1	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	54	5	8	2	0	81	8	6	0	4
Non-respiratory		1	4	1	0		2	7	0	0
Whooping-cough	2	0	0	0	0	5	1	2	0	0
Deaths 0–1 year	181	28	16	8	9	168	20	24	8	13
Deaths (excluding stillbirths)	4,114	587	459	86	137	4,312	584	476	97	149
LIVE BIRTHS	7,636	1177	805	220	336	7,803	1157	907	219	378
STILLBIRTHS	211	31	28			166	19	20		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

B.M.A. Gold Medal.—Sir HENRY SIMPSON NEWLAND was invested with the Gold Medal of the British Medical Association by Dr. A. TALBOT ROGERS, on behalf of the Council of the Association, at a ceremony in Sydney on August 25. The citation states: "In deep gratitude for your outstanding and devoted services, the Council of the Association now asks you to accept the highest distinction within its gift." Sir Henry Newland helped to establish the Royal Australasian College of Surgeons, of which he was president from 1929 to 1934. He is also a past president of the Federal Council of the B.M.A. in Australia.

Report on Cutter Vaccine.—On August 25 in New York the United States Public Health Service made public its report on its investigations into the production and testing of the Cutter poliomyelitis vaccine (see *Journal*, June 18, p. 1485). Of about 400,000 American children inoculated with the Cutter vaccine, 73 developed poliomyelitis within 31 days of inoculation, and the injection site was the first site of paralysis in a high proportion of the cases. Discussing the report with the Press, Dr. LEONARD SCHEELE, Surgeon-General of the Public Health Service, is quoted as saying that the "exact reasons" why live virus had persisted in the vaccine had not been discovered. While refusing to exonerate completely the Cutter Laboratories, Dr. Scheele put the main blame for the "Cutter incident" on the failure of the Government's safety tests.

Employment and Management of the Cardiac Patient.—Two years ago the British Council for Rehabilitation set up an expert working party, under the chairmanship of Dr. WILLIAM EVANS, to consider the facilities for cardiac patients. Its brief included a reference to both treatment and subsequent employment, and asked for recommendations. The working party's report, which has now been published, discusses the problem as it presents in the child, the young adult, and the elderly cardiac patient. In an important section on the avoidance of unwarranted invalidism in children stress is laid on the need, first, for accurate clinical assessment, and secondly, where the presenting sign is innocent, for this information to be "conveyed emphatically to those concerned." The working party proposes that medical officers of health should maintain lists of those children in whom heart disease has been diagnosed or suspected by school medical officers, and that these children should be investigated by a cardiologist named by the British Cardiac Society. If the physical signs are of no moment, it should be the duty of the cardiologist to interview the parent and explain the situation, as well as notifying the patient's practitioner and the M.O.H. (and hence the school medical officer). The cardiac department should also be responsible for following up the case to make sure that the reassurance has been acted upon both at school and in the home. The report recommends that local general practitioners should be informed of the facilities available in the department, and be invited to refer to it children with heart disease. A final recommendation is that alternative superannuation schemes should be inaugurated for cardiac patients engaged in occupations where at present they are debarred from such benefits on account of their ailment. Besides the chairman, the working party included six doctors—Dr. R. E. BONHAM CARTER, Dr. A. THELWALL JONES, Dr. PAUL WOOD, Dr. SAMUEL ORAM, Dr. J. W. BROWN, and Dr. D. M. WILLIAMSON. Copies of the report (free, postage 1½d. each) may be obtained from the British Council for Rehabilitation, Tavistock House (South), Tavistock Square, London, W.C.1.

International Society of Plastic Surgeons.—During the First International Congress of Plastic Surgery last month in Sweden an International Society of Plastic Surgeons was formed, with Sir HAROLD GILLIES as its honorary president. Its objects are "to promote plastic surgery both scientifically and clinically; to further education; and to encourage friendship between physicians in all countries." The Society

has both "society" and "congress" membership, the former being restricted to those specializing in plastic surgery or related fields, while the latter is open to any interested medical practitioner as well as to relatives or friends accompanying a "society" member. Congresses will be held every fourth year. The society's business will be conducted by an executive committee appointed by the general assembly at the quadrennial congresses, a council consisting of one delegate from each national association of plastic surgeons, and the general assembly of all attending "society" members. In addition to the honorary president, the following other officers were elected at the Congress: general secretary, TORD SKOOG (Sweden); treasurer, KARL HOGEMAN (Sweden); executive committee, TRUMAN BLOCKER, Jr. (U.S.A.), FRANCIS BURIAN (Czechoslovakia), MARIO GONZÁLEZ (Mexico), Sir ARCHIBALD MCINDOE (Great Britain), DANIEL MOREZ-FATIO (France), GUSTAVO SANVENERO-ROSSELLI (Italy), and KARL SCHUCHARDT (Germany).

Austrian Doctors Strike.—Austrian doctors and dentists carried out a nation-wide strike on August 25 and 26 in protest against some of the provisions of a proposed new social insurance law, due to be considered shortly by the Austrian parliament. According to newspaper reports, the Austrian Chamber of Doctors, after arranging a skeleton service of some 3,000 doctors to deal with emergencies, called upon the remainder of its 13,000 members to stop work, and the Austrian Chamber of Dentists did likewise. In Vienna motorized columns of doctors toured the city, distributing pamphlets explaining their views and visiting health insurance hospitals and clinics. There were some incidents with the police. One of the objects of the new measure is to regulate the doctors' relations with the autonomous health insurance bodies. It seems that the doctors' principal grievance, states *The Times* correspondent in Vienna, is the proposed unrestricted right for the health insurance bodies to dismiss individual doctors without explanation. Other demands include the right of all doctors to participate in the health insurance scheme, better remuneration, and financial contributions to treatment by insured persons above a certain income level.

London University and Overseas University Colleges.—Certain overseas university colleges, such as the University College of the West Indies and University College, Ibadan, have been accepted into "special relation" with London University. This is accorded only after a satisfactory report to the Senate of London University on the college's academic status and constitution. Students at these colleges then become eligible for the "special relation" degrees of London University, once the course of instruction for the particular degree has been approved. The degrees are of the same standard as the usual London degrees, but the syllabuses may be modified to suit local conditions. A Senate committee watches over the progress of these colleges, and in its report of the 1954–5 session records the graduation of the first group of M.B., B.S. students at the University College of the West Indies. A warm tribute is paid to Dr. T. C. HUNT, of St. Mary's Hospital, who played a large part in the work of establishing a teaching hospital in Jamaica. The report also records that, of the 11 students from Ibadan who came to Britain for their clinical studies (a teaching hospital is at present being constructed in Ibadan—see *Journal* of November 27, 1954, p. 1303), nine were successful in the Internal London M.B., B.S. finals.

Society of Apothecaries of London.—Dr. NEVILLE FINZI was elected Master of the Society of Apothecaries in succession to Sir CECIL WAKELEY at a meeting of the Court of Assistants on August 16. Dr. MACDONALD CRITCHLEY and Dr. REGINALD FISHER were elected Wardens, and Dr. KENNETH PERRY was appointed examiner in medicine in succession to Dr. NEVILLE OSWALD, who has resigned.

Research on Ageing: Ciba Foundation Awards.—The Trustees of the Ciba Foundation announce five awards for 1955–6, of average value £300, for reports of research "relevant to basic problems of ageing." Reports should not exceed 7,000 words in length, and the last date for their receipt is February 10, 1956. The results will be judged by an international panel of distinguished scientists. Further details from Dr. G. E. W. WOLSTENHOLME, Ciba Foundation, 41, Portland Place, London, W.1.

Standard Scalpels.—The British Standards Institution has issued for comment a draft British Standard for surgical scalpels (CV(SGC)6346). The draft was prepared by the Institution's Surgical Cutting Instruments Committee, whose chairman is Sir HENRY SOUTTAR. Any comments on the draft standard should be sent to the British Standards Institution, 2, Park Street, London, W.1, not later than October 7.

Consultant Psychiatrist to the Army.—Dr. R. F. TREDGOLD has been appointed honorary consultant in psychiatry to the Army at home in succession to Dr. J. R. REES. Dr. Tredgold holds appointments as regional psychiatrist to the South-east Metropolitan Regional Hospital Board and physician to the department of psychological medicine at University College Hospital, London.

Dr. Frank Falkner, lecturer in child health at the Institute of Child Health, Great Ormond Street, and coordinating officer to the Centre International de L'Enfance, Paris, for their international growth studies of children, will take up an appointment as assistant professor of child health at Louisville University, Kentucky, in January. Dr. Falkner will retain his Paris appointment, and one of his tasks will be to initiate a growth study in Kentucky, as so far there is no North American contribution to this investigation.

COMING EVENTS

Radio and Television.—Spiritual healing: an inquiry (Sunday, September 4, Home Services at 9.15 p.m.). "Atoms for Peace": report by Professor J. ROTBLAT (St. Bartholomew's Hospital Medical School) on Geneva Conference (Tuesday, September 6, television at 8.45 p.m.).

International College of Surgeons.—The following meetings have been arranged, details being obtainable from Dr. JAMES F. BRAILSFORD, 20, Highfield Road, Edgbaston, Birmingham, 15: September 12–15 at Philadelphia; October 12–16 at Belo Horizonte, Brazil; October 22–23 at Vienna; October 22–26 at Mendoza, Argentine; October 30 at Tokyo; and November 18–20 at Amsterdam.

Tuberculosis Course.—Postgraduate course for general practitioners at Royal Berkshire Hospital, London Road, Reading, and Peppard Chest Hospital, Henley-on-Thames, week-end October 22–23. Details from Tuberculosis Educational Institute, Tavistock House North, Tavistock Square, London, W.C.1.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bailey.—On August 15, 1955, at Port Elizabeth, South Africa, to Sheila (formerly Watts), M.B., B.S., wife of Robert Anthony Bailey, F.R.C.S., a son.

Baird.—On August 21, 1955, at Jessop Hospital, Sheffield, Yorks, to Ivy (formerly Hayhurst), wife of Ian McLean Baird, M.B., M.R.C.P., a daughter—Fiona.

Lovel.—On August 22, 1955, at 27, Cedar Road, Sutton, Surrey, to Joan (formerly D'Arcy), M.D., D.C.H., and Lester Lovel, of Banstead, Surrey, a daughter—Mary Patricia.

Pettitt.—On August 18, 1955, at Weir Maternity Hospital, London, S.W., to Helga, wife of Dr. G. C. Pettitt, of Sydney, Australia, a son—Martin Charles Gordon.

Pillai.—On June 21, 1955, at Swansea, to Lenora (formerly Anthony), wife of S. Pillai, M.B., F.R.C.S., a sister for Mohan Anthony—Karen Indira.

Rigby.—On August 20, 1955, at the Royal Victoria Hospital, Boscombe, Hants, to Dina (formerly Bowen), wife of Philip Rigby, M.B., Ch.B., 24, Sycamore Road, Handsworth, Birmingham, a son—Peter Wesley.

Turner.—On August 5, 1955, at Shearwood Nursing Home, to Dr. Naomi (formerly Myers), wife of Dr. M. H. Turner, of 1, Victoria Road, Sheffield, 10, a daughter—Deborah Celia.

MARRIAGES

Abrahamsson—Oliver.—On August 9, 1955, at The Oratory, Bengt Paul Abrahamsson to June Marie Oliver, M.B., Ch.B., D.A. Address: Nybrogatan 5, Eskilstuna, Sweden.

DEATHS

Grant.—On August 17, 1955, at 82, Graham's Road, Falkirk, Stirlingshire, Robert Grant, M.B., Ch.B.

McEwan.—On August 17, 1955, at 7, Palmeira Square, Hove, Sussex, Mary McEwan, M.R.C.S., L.R.C.P.

Prosser.—On August 8, 1955, Frank Atkinson Prosser, M.B., Ch.B.

Speirs.—On August 8, 1955, at Fairfax House, Colton, Hovingham, York, James Miller Speirs, L.R.C.P., L.R.C.S., late of 119, Wortley Road, Leeds.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Swollen Ankles in Hot Weather

Q.—*During the recent warm weather, as in previous years, I have been seeing several cases of oedema of the ankles, always in women, mostly in girls of 17–21 age group. In the absence of renal disease, with a normal Hb and E.S.R., no cardiac disease, and no varicose veins, what is the likely cause of the condition? How should these patients be investigated in order to establish the cause?*

A.—This condition is not uncommon. An increase in the environmental temperature is associated with an increase in the rate of formation of tissue fluid in the limbs. The tissue fluid is, of course, produced by filtration from the blood across the capillaries; when the body is warmed, vessels of the limbs dilate and the total filtering surface increases; this has been held to account for the increase in tissue fluid. When vasodilatation is produced by sympathectomy there is also an increase in the formation of tissue fluid in the limb. It is admittedly difficult to see why the filtered fluid should then accumulate, and it is possible that a change in the environmental temperature increases the volume of the extracellular fluid of the whole body. At all events, it is doubtful if the swelling is, in fact, limited to the ankles—the hands probably swell too—but with much standing fluid is aways more likely to accumulate in the lower limbs. The condition is not of course limited to young girls, but they may be more aware of a change in the shape of their ankles. Also the swelling may be more obvious in them than in men, if it happens at the same time as a premenstrual retention of water.

It is unlikely that any investigations need be undertaken for clinical purposes, as the swelling seems to disappear even if the weather continues warm, and it has no pathological significance. It would be interesting to know how much the body weight increases, as this would give some idea whether the accumulation of fluid is limited to the extremities.

Face Powder and Sunburn

Q.—*Could you suggest a prescription for a face powder to give protection against sunburn? Would such a powder offer any protection against flashburn from an atomic explosion?*

A.—The sunburn protective properties of face powder were recently reported by A. D. Porter.[1] In his experiment he used a powder consisting of talcum 58%, prepared chalk 5%, zinc stearate 10%, and fuller's earth to 100%. This may be tinted to obtain the appropriate shade by adding small quantities of ferric oxide, carmine, and orange G. When this powder was applied—in the same manner as an ordinary cosmetic face powder on top of a non-protecting face cream—it doubled the light tolerance of the skin. The experiments were carried out on a patient who was abnormally sensitive to light, but the same result may be expected in a normal person. The addition of 3% quinine sulphate to this powder increased the light tolerance by a further 50%. At the same time it was found that an ordinary cosmetic face cream and powder, as regularly used by that patient, was almost as effective. The effectiveness of cosmetic face powder depends partly on its "covering" power, which is much the same as saying it depends on the powder's opacity to light. It is therefore not surprising that an ordinary cosmetic face powder will protect the skin against the sun fairly efficiently. Some bismuth salts have a good covering power, but barium is perhaps best avoided because of possible irritancy.

The chief drawback to the use of face powders as a protection against sunburn is that they wash off—a considerable drawback for sun-bathers on the beach; they need to be liberally applied, which may be all right for women but is not practicable for men; finally, it must be remembered that the use of protective substances prevents the development of natural tolerance, so that the skin may eventually become even more sensitive to the sun than usual.

Protection against flashburning is a different matter, since the radiation concerned is of a very different wavelength from that causing ordinary sunburn, and I am not aware of any experimental work relating to that.

REFERENCE

[1] *Brit. J. Derm.*, 1954, **66**, 417.

Hydrocortisone Ointment in Allergic Dermatitis

Q.—*I would be obliged if you would give me the following information on the use of 1% hydrocortisone ointment in allergic dermatitis. (1) Are there any contraindications or complications? (2) Can treatment be maintained indefinitely, if exposure to the allergen is rendered necessary by the patient's work?*

A.—There are no contraindications or complications to the use of hydrocortisone ointment. Very rarely a patient has shown intolerance to the base of the ointment. In theory this treatment might favour secondary infection, but in practice this is rarely seen.

Treatment can be maintained indefinitely, but is likely to be ineffective in the continued presence of the offending allergen, even if repeated applications are made. Successful treatment would seem to call for removal of the allergen or effective protection against contact.

Vitamin Supplements for Babies on Dried Milk

Q.—*The quantities of vitamins A and D in dried milk should be sufficient, theoretically, for an infant's requirements. Is it necessary, therefore, in babies fed on dried milk, for the mothers to give cod-liver oil or other preparations containing vitamins A and D? Is it possible for early rickets to develop in a child receiving dried milk alone?*

A.—The baby's daily vitamin-A requirements are between 2,000 and 4,000 international units, and a normal baby obtains sufficient from cows' milk to cover his needs. It is a heat-resistant vitamin, and therefore not appreciably affected by boiling or drying. Disorders due to vitamin-A deficiency are almost unknown in this country in infancy. It is possible that some degree of deficiency might occur in ill babies or those with steatorrhea.

The infant's requirements of vitamin D have been variously estimated to be between 500 to 1,000 international units per day, and most dried milks are now fortified with an additional 280 to 300 units per ounce (28 g.) of the dried milk. A baby who is taking 16 fl. oz. (535 ml.) or more of the milk, made up to full strength (2 oz. (56 g.) of the powder), or the equivalent of diluted milk, will be receiving sufficient to cover its requirements. Rickets will not develop in such a case. The natural vitamin-D content of milk is more variable than the vitamin A, and the added vitamin D in dried milk makes up for this. There is, however, not a great margin for the baby who is refusing milk or vomiting a large proportion of it, or who has started on a mixed diet and is not taking enough milk or fortified cereal to cover the daily requirements of vitamin D. The real advantages of the daily supplement are that, firstly, it covers the need of all children whatever the vagaries of their daily diet, and effectively prevents any deficiency arising. Secondly, it is much easier to start the habit of a daily spoonful of oil in babyhood than it is later, and during that period there are opportunities for teaching mothers to do this which do not arise later. The need for an ample intake of vitamins A and D is after all just as great or greater during early childhood as it is in infancy, and, as the dietary intake may then be deficient, the habit of a daily supplement becomes more important.

In summary, then, from the narrow point of view any individual baby receiving an adequate amount of dried milk does not need a further supplement of vitamins A or D. From the point of view of babies and older children in general the daily supplement is a wise and necessary precaution in this country.

Treatment of Coccydynia

Q.—*What treatment is advised for severe coccydynia following a bad injury 9 months ago in a man of 45? There is no radiological evidence of fracture.*

A.—Coccydynia is an ill-understood condition and knowledge of its cause and treatment is negligible. It is much commoner in women and usually follows a fall, but there is virtually no radiological change.

Treatment by local physiotherapy such as short-wave diathermy, manipulation under anaesthesia, and injection of various local analgesic agents are all tried, sometimes with success, sometimes without; in fact many of the cases recover spontaneously. Sometimes protection by a felt ring to relieve the pain when sitting is useful. Finally, not a small group who continue to get pain over many months or years have to be considered for more radical treatment—that is, excision of the coccyx. This again is often a failure and is best not carried out as a line of treatment, for the following reason: Recently it has been suggested that coccydynia is a manifestation of a disk prolapse, and on this view a belief has been expressed that the logical treatment is a plaster jacket. There is some evidence in favour of this, but the theory cannot yet be regarded as well established.

Coccydynia is sometimes a psychological manifestation, or becomes one, and in women it is usually associated with sexual difficulties. It is not uncommon to find that in coccydynia there is frank hysteria, though this is not to be understood to mean that all cases of coccydynia have a psychological background.

Amenorrhoea in a Healthy Woman

Q.—*Is it necessary to treat amenorrhoea in a woman who is otherwise entirely healthy, at least so far as any ordinary physical examination can determine? Three or four times I have come across women, say, of 32 to 38, who have had long periods of amenorrhoea, obviously not related to a premature menopause, and who all seemed to be active and healthy, whose medical treatment had made them introspective. Apart from the question of child-bearing, is it really of great importance that all cases of amenorrhoea should be treated?*

A.—The only justification for treating amenorrhoea *per se* is from the standpoint of the woman's fertility. Otherwise specific hormone therapy is not only unnecessary but may be harmful, as is suggested in the question. A reasonable explanation of the situation and assurance that it does not result in ill-health are enough in many cases. Nevertheless, amenorrhoea of significant duration in a woman aged 18 to 40 years should not be dismissed, even though she is apparently well, until a full investigation has excluded causal organic diseases. Indeed, without this the necessary reassurance cannot be given. Tuberculosis of the lungs or genitalia, diabetes, tumours of the ovary, adrenal, and pituitary, or lymphadenoma, for example, can be remarkably silent, and may at first present no obvious clinical manifestations except amenorrhoea.

Choice of Local Analgesic

Q.—*What determines the choice of the local analgesic for (a) minor operations on the fingers, (b) infiltration of the abdominal wall before major surgery? Which are recommended and in what strength? Is lignocaine suitable for infiltrating the abdominal wall of babies undergoing operation for pyloric stenosis? If so, what dilution is recommended?*

A.—The choice of drug for local analgesia is determined by its toxicity and the desired duration of analgesia. The drugs of low toxicity in common use are procaine and lignocaine. They are each used in dilutions of ½–1%, with 1 g. (200–100 ml.) as an average maximum dose for a healthy adult. Analgesia will last up to 1½ hours with procaine and up to 3 hours with lignocaine. In each case adrenaline is added to the solution in a concentration of 1 in 200,000.

In the case of minor operations on the finger, 1% procaine is quite satisfactory, while the longer lasting, more diffusible, lignocaine in a strength of ½% would be more suitable for infiltration of the abdominal wall. It has been said that there is a risk of gangrene of a finger if adrenaline is used, and, whilst this possibility is somewhat conjectural in the healthy adult, it is better to omit adrenaline from the solution in this situation. As the operation is usually a very short one, the limited duration of anaesthesia due to omission of adrenaline will be no disadvantage. Lignocaine is quite suitable for infiltration of the abdominal wall of babies for operations for pyloric stenosis. A dilution of ½% is recommended, not more than 20–30 ml. of the solution being injected.

Clinical Diagnosis of Non-paralytic Poliomyelitis

Q.—*On what clinical signs and symptoms is it possible to found a firm diagnosis of non-paralytic acute poliomyelitis?*

A.—It is necessary to say at the outset that in many cases the clinical diagnosis can never be "firm" and must often indeed be little more than a guess. Sometimes it is true the illness will run the typical biphasic course of the paralytic disease except that paralysis does not develop. There will be fever, headache, vomiting, slight nasopharyngeal irritation, and general lassitude. This will be recovered from, to be followed by a secondary febrile illness in which intense headache, irritability, and neck and back stiffness are the main features. In such cases the cerebrospinal fluid will usually show typical changes. But at the other end of the scale there will be many persons who show little more than fever and headache with perhaps some neck stiffness. It is a general experience that the close eliciting of family histories before and for 2–3 weeks after a typical case of polio has occurred will show a high incidence of febrile illness which it seems likely is due to the polio virus. It is indeed the occurrence of an actual case which livens the doctor's awareness so that in epidemic areas the diagnosis is more frequently made. The diagnosis of acute poliomyelitis is discussed in more detail in a recent article by Dr. T. Anderson.[1]

Probably most of the cases of non-paralytic polio which appear in the notification reports are those which are observed in hospital either originally sent in as polio or more often with other diagnoses. The figures as such mean very little, and one suspects that this vague title covers a variety of virus illnesses involving the central nervous system. As it becomes possible by accurate virological techniques to diagnose these illnesses more exactly, it seems likely that we will find that other viruses are involved and that, like influenza, the clinical diagnosis is most inaccurate.

REFERENCE

[1] *British Medical Journal*, 1955, **2**, 485.

Treatment of Sunburn

Q.—*What is the best treatment for sunburn?*

A.—It is presumed that the question relates to ordinary seaside-holiday sunburn. The best treatment is, of course, prevention by gradual exposure, or by the use of protective lotions or creams, such as calamine lotion or lanolin. Once burnt, mild reactions are soothed by calamine lotion or cream. More severe reactions with oedema, redness, and burning, and later peeling of the skin, call for rest, and are soothed by the following application: zinc oxide ointment, to which has been added 1 dr. (3.9 g.) sulphur ointment (*N.F.*) to the ounce (31 g.).

If there is vesication or blistering, cold (boiled) water compresses, or cold lead lotion, followed by the cream will give comfort most quickly. If the burns are more severe than this, they should be treated as ordinary burns of major degree.

Antibiotics for Holiday in Hot Climate

Q.—*I am about to undertake a motor tour in Yugoslavia, and should like to take a supply of antibiotics which would deal with as wide a variety of infections as possible. I believe the heat in summer is so great that it would be necessary to take a very stable compound in the absence of refrigeration facilities. What would you recommend?*

A.—Antibiotics in the dry solid form are not materially affected by short periods in a hot climate: the stability factor need therefore not affect the choice made.

The commonest ailment during a holiday abroad is diarrhoea, and for treating this, if it is severe enough to suggest a dysenteric or other such infection, it is usual to take one of the less soluble sulphonamides, such as sulphaguanidine. Possible indications for antibiotics are septic infection of skin or wounds, acute sore throat, and pneumonia. Most of the bacteria likely to be responsible for any of these conditions are sensitive to the tetracyclines, and whichever of these is preferred would be a useful all-purpose drug in these circumstances.

Disinfection of a Leprosarium

Q.—*It is desired to convert a 200-bedded leprosarium into a tuberculosis hospital, as there are now so few lepers in this area. After the departure of the lepers, what disinfection is necessary to make the hospital safe for the reception of other patients?*

A.—As the leprosy bacillus cannot be cultured *in vitro* and cannot infect experimental animals, we have no exact knowledge of its viability. We know, however, that it is of low infectivity, probably much lower than that of the tubercle bacillus. So it is safe to say that any method sufficient to disinfect buildings from tuberculosis would be more than sufficient to disinfect from leprosy. Much depends on the nature and condition of the buildings. If of wood, then thorough washing with a detergent, followed by repainting of the walls, should be sufficient. If of stone or brick, then thorough mending, replastering, and whitewashing of the walls and ceilings, with mending and washing of the floors, would be sufficient. Certainly thorough steps should be taken to exterminate all vermin. There is reason to believe that light and drying is as fatal to the leprosy as to the tubercle bacillus; but it may be taken for granted that there is plenty of light and sufficient ventilation in a building suitable for use as a tuberculosis hospital. The surroundings of the buildings should also be thoroughly cleared.

NOTES AND COMMENTS

Side-effects of Stilboestrol.—Dr. R. AIDIN (Worthing) writes: In describing the side-effects of stilboestrol your expert (*Journal*, July 23, p. 276) does not mention its anti-atherogenic effect. For some years in doing routine necropsies I have noticed the relative absence of atheroma in the aorta and coronary arteries in subjects that have been treated with stilboestrol for prostatic carcinoma when compared with other male subjects of the same age group. My figures are too few to be statistically significant; Rivin *et al.*[1] have seemingly proved the anti-atherogenic effect of stilboestrol in a carefully controlled biometric study. A point not noted by these authors but observed by me is surprising—the aortas of stilboestrol-treated subjects seem to have regained the elasticity of youth. Some physicians are treating with stilboestrol patients who are recovering from coronary occlusion or thrombosis. Perhaps this side-effect may become of importance in the treatment of a common and disabling condition.

REFERENCE

1 Rivin, A. U., and Dimitroff, S. P., *Circulation*, 1954, **9**, 533.

OUR EXPERT replies: There is considerable evidence to support the view that oestrogens have an anti-atherogenic effect. The work quoted by Dr. Aidin is a good example. There is also convincing work on record that plant sterols—for example, sitosterol—prevent atherosclerosis. A number of people have maintained that the serum cholesterol can also be reduced by this substance. After the war androgens were much in vogue for the treatment of angina pectoris, and from the enthusiastic reports one might have thought that they were the solution to this problem. However, no one uses them now. Strangely, there seems to be no record in the literature from 1945 up to now of stilboestrol being used in the treatment of cardiac infarction.

Treatment of Ulcerative Colitis.—Dr. ROBERT W. DOY (Stony Stratford, Bucks) writes: May I be permitted to comment on the answer given under the heading of "Any Questions?" (July 23, p. 276) regarding recent advances in the treatment of ulcerative colitis? I am sure there is no need to draw your expert's attention to the work of numerous physicians and psychiatrists on the use of psychotherapy in this disease, but I am surprised that he did not see fit to refer to it in his reply. Although a psychoneurotic background in many cases of ulcerative colitis has been appreciated for many years, much of the work can fairly be classed as "recent." If your correspondent is at all interested in this aspect of treatment, may I recommend to him the short but useful article by Groen and Bastiaans in *Modern Trends in Psychosomatic Medicine*, edited by Desmond O'Neill (Butterworth, London, 1955), which includes an extensive bibliography?

Progressive Asthma.—Dr. C. E. HAGENBACH (Bath) writes: In your reply ("Any Questions?" July 2, p. 73) paraldehyde was suggested for sedation. Paraldehyde gives a most objectionable odour to the breath. Would not methylpentynol be equally effective and without this disadvantage?

OUR EXPERT replies: Paraldehyde has for many years been acknowledged as the safest hypnotic in asthma and as such has been widely used. The use of methylpentynol in asthma was the subject of a very recent article in the *Journal*.[1] It is far too early yet to suggest that methylpentynol will be as effective and safe as paraldehyde.

REFERENCE

1 Bendkowski, B., *British Medical Journal*, 1955, **2**, 297.

"Fluorescent Perspex."—Dr. D. KENWIN HARRIS (Plastics Division, Imperial Chemical Industries Ltd.) writes: The reply to the problem of dermatitis caused by fluorescent "perspex" acrylic sheet mentioned under "Any Questions" (July 30, p. 338) is not altogether correct. It is true that there are traces of free monomer in perspex sheet which may be liberated under certain conditions. If the material is finely disintegrated, for example, and sprayed on to the skin as a powder, the monomer may be responsible for any subsequent irritation, but this could also be due to decomposition products of the polymerized material itself. The references to benzoyl peroxide are irrelevant so far as this country is concerned, since it is not the catalyst employed in the manufacture of fluorescent perspex sheet. Lastly, there is more than one additive present in amounts that represent a very small percentage of the final product. These additives, however, are firmly contained within the polymerized substance, and so little is likely to be set free that in my opinion they are a most improbable cause of the skin irritation.

Corrections.—We regret that the name of Mr. S. W. Allinson, of Boston, Lincolnshire, was wrongly spelt in our report of the meeting of the Section of Otolaryngology in Toronto on June 22 (July 9, p. 126).

It is regretted that in the article on "The Whitfield Tradition of Therapy" (August 20, p. 453) the amounts of salicylic and benzoic acids in two of the prescriptions were given in minims instead of grains. The prescriptions should have been: *Whitfield's lotion for fungus infections of the feet.* Benzoic acid 180 gr. (11.7 g.), salicylic acid 120 gr. (7.8 g.), acetone 2 fl. oz. (57 ml.), industrial methylated spirits to 8 fl. oz. (230 ml.). *Whitfield's lotion for warts.* Mercury biniodide 2 gr. (0.13 g.), salicylic acid 60 gr. (3.9 g.), 70% spirit to 1 fl. oz. (28 ml.). In the *zinc and ichthyol cream prescription for pruritus ani* the zinc oxide content should have been ½ oz. (31 g.).

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